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MAN — AN ADAPTIVE MECHANISM

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MAN—AN ADAPTIVE MECHANISM

BY

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To

A COLLABORATOR

GRACE McBRIDE CRILE

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PREFACE

For more than twenty years, the general theme treated in this volume has been under investigation in my laboratory and my clinic, and the volumes published during that time have recorded the steps by which I have approached the theories here presented.

The accumulated experimental and clinical data are so extensive that summaries only are given in the present volume, which is an argument for the main thesis, that man is essentially an energy-transforming mechanism, obeying the laws of physics, as do other mechanisms. In presenting this thesis, certain hypotheses have been freely employed where the data were insufficient that they may furnish a working basis upon which to accumulate additional data. An hypothesis — incomplete or even false — is so easily demolished that it can do little harm; while the presentation of a "false fact" may produce pernicious results.

To no one are the imperfections and shortcomings of this presentation more apparent than to the author, who lays no claim to expert knowledge in any one of the several sciences involved in attempting a synthesis of such wide scope.

A review of the literature and the details of most of the researches whose conclusions are used in this

volume are not included here, but will be published elsewhere. Our difficulties and the shortcomings in our argument will be obvious enough even when relieved from references to a massive literature.

The work of the laboratory, which since the beginning of the research has included some 2500 experiments, has as far as possible been checked and illuminated at every step by the clinical observations made by my associates, Dr. Lower and Dr. Sloan, and by myself.

The result of this research, as here presented, is the combined outcome of a large amount of work and enthusiasm on the part of many associates. It represents a generous contribution, not only of labor, but of valuable suggestion and criticism from colleagues and friends, to whom I wish here to express my gratitude.

I am deeply sensible of my obligations to Sir Victor Horsley for the opportunity of beginning this research in his laboratory in 1895; and for many valuable suggestions and criticisms; to Professor Sherrington for reading the original manuscript on "Phylogenetic Association"; and to Professors G. N. Stewart, W. T. Howard, T. Sollman, and J. J. R. MacLeod of the Western Reserve Medical School, all of whom have generously given me the benefit of their wide experience and scientific knowledge.

To the following laboratory and clinical associates I acknowledge my gratitude and indebtedness for assuming much of the burden of experimental details: Dr. Guy H. Fitzgerald, Dr. A. Cudell, Dr. Homer H. Heath, Dr. C. H. Lenhart, Dr. Worth Brown, Dr.

Clyde E. Ford, Dr. H. P. Cole, Dr. D. A. Prendergast, Dr. A. B. Eisenbrey, Miss O. M. Lewis, Dr. A. M. Tweedie, Dr. Lawrence Pomeroy.

To Dr. David H. Dolley, Dr. F. W. Hitchings, and Dr. J. B. Austin I wish particularly to express my deep appreciation of their long, painstaking, and enthusiastic service in the laboratory; and for bearing the burden of the major portion of the experimental details. I am indebted to Dr. Dolley for making for me the histologic studies of the brain in shock and emotion; to Dr. Hitchings for prolonged and extensive work in every branch of the research, particularly for his work on the adrenals; for a critical review of the literature; for devising a method of making actual Purkinje cell counts; and for compiling, analyzing, and tabulating the large mass of experimental data; to Dr. Austin for painstaking work on the histologic changes in the organs and tissues of man and animals, and especially for his extensive histologic study of the brain, which has included the counting and classifying of over one hundred thousand brain-cells; to Dr. H. G. Sloan for assuming many of the operative details; for the physiological investigation of the adrenals, and for other clinical and research work; to Dr. Maud L. Menten for her researches upon the adrenals, the electric fish, and the H-ion concentration of the blood, in its relation to the factors causing exhaustion and death.

My thanks are due to Dr. Austin and Mr. John E. Olivenbaum for making the photomicrographs; to Mr. W. J. Brownlow for original drawings and photographic studies; to Miss Amy F. Rowland for

collaboration in the research upon the chemical constituents of various organs of animals under conditions of activation; and to Dr. W. J. Crozier for reading the manuscript and for valuable suggestions.

To my associate, Dr. W. E. Lower, I am heavily indebted for the invaluable assistance he has given me throughout the entire research

To Miss Annette Austin I wish to express my special appreciation of her great assistance in compiling the data from my various monographs, manuscripts, and papers, as well as from the literature; and of her aid in their presentation in the following pages.

GEORGE W. CRILE.

Cushing Laboratory of Experimental Medicine,
Western Reserve University,
January 1, 1915.

[redacted]

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INTRODUCTION

I

With the advance in natural science, which was inaugurated by the general acceptance of Darwin's theory of evolution, a tendency has developed to regard health and disease alike as natural phenomena subject to the same laws as those which govern other physical processes.

If man, like other animals, is the product of evolution, then his existing form and the functions of his various organs and tissues must have been determined by that age-long struggle. Disease, the failure of the organism to adapt itself completely, and health are alike expressions of natural processes — comprehensive terms which designate the net result of many trials of interacting, imperfect mechanisms, evoked by nature's emergencies, and accepted, suffered or cast off, as they have proved useful, harmful or ineffective in the combat, but all working in common, in sickness or in health, toward a more complete adaptation to environment.

The conception that the struggle for existence is the sole determinant of the outer form and inner processes of man's body gives a new meaning to the problems of disease. Each organ, each function assumes a new, often a tragic, value in the light of its rôle in the drama of adaptation. The inadequacy of some of nature's methods and the perfection of others are shown in these complex and unbalanced problems of health and disease, the solution of which may be attained by medical skill when properly equipped through study of the part played by each mechanism in the history of the species.

The impetus which the theory of evolution has imparted within the last sixty years to biology, to chemistry, to physics, to geology, to astronomy, in fact, to every natural science, has never before been equaled. In view of this fact that most sciences have availed themselves fully of the opportunity offered by the doctrine of evolution to coördinate their data, it seems odd that medicine should have lagged so long to find inspiration in its revelations.

The tardiness of the medical profession in making use of the theory of evolution has not been because that profession did not need a coördinating working basis. The delay may perhaps be traceable to the fact that, unlike other scientific studies, medicine has been closely associated in every age with the everyday life of the people, its prime object being to relieve suffering. The public has always demanded definite, finished results, and, as scientists know, definite and final conclusions are usually incompatible with tru science. It has never been possible for medicine

be truly scientific in the sense of being neutral, exact and unbiased. Developing as it has, as a sort of household necessity, and lacking the resources of assured scientific data or the support of coördinated methods, it is no wonder that it is even now in a somewhat chaotic state.

That a change of viewpoint will follow the present liberal advance in medicine is probable. All progress indicates the early formulation of a synthetic basis upon which the problems of many diseases may be rationally resolved. Medicine has been for a long time at the parting of the ways. Like other sciences, it has had to evolve through the three traditional stages of development: a stage of superstition and empiricism; a stage of experiment and accumulation of data; and a final stage of synthesis and coördination of facts. That medicine is well through the second stage and has entered the final stage of synthesis in which practical working principles are being formulated is evidenced especially by the increasing control of infectious diseases. In many instances the older volumes filled with dissertations on certain diseases contain less useful information than now is comprised in single sentences or words which indicate both origin and control. With malaria and yellow fever explained by one word, *mosquito;* diphtheria reduced to *bacillus* and *anti-toxin;* smallpox disposed of in *vaccination;* bubonic plague apprehended in *infected vermin;* and synthetic chemistry producing such a specific as *salvarsan;* there is hope for a like conquest of the host of chronic diseases, and fairer promise for a future of preventive medicine.

The old restricted viewpoint, which led pathologist and clinician to regard disease as an isolated phenomenon, unrelated to the normal processes of the body, is giving way to the more enlightened view that disease is related to every factor in the life of the species. The logical step from this conclusion is to an inquiry into the past, as well as the present environment of the species. Medical progress, which began with the study of dead forms and gained a great impulse from the observation of living processes, is now face to face with the necessity for making a complete biologic picture of the evolution of both the form and the functions of organisms. Phylogeny, or the study of the ancestral life of species, will probably play a more important rôle in future medical research.

Had Darwin and Herbert Spencer applied the principle of natural selection to physiology as completely as the former applied it to anatomy and to gross behavior, they would undoubtedly have left to us an important compilation of data, thus establishing the basis for a constructive theory of medicine, such as medicine has never possessed. Had either Darwin or Spencer applied the fundamental principle of continuity of development to the functions as well as to the structure of the organism, we should have been saved from much of the confusion which has resulted from the old arbitrary division of organic processes into "physical" and "psychical." There is no doubt that this unscientific division has delayed the solution of those medical problems which are primarily concerned with nervous processes.

Every step toward the truth makes more evident the fundamental unity of natural phenomena and help

to dissipate the false distinctions which have been the outgrowth of imperfect understanding of facts which were made more obscure by dogmatic definitions.

II

The present volume is the outcome of an effort to harmonize a large amount of clinical and experimental data by the application of certain biologic principles, these data having been collected in the course of researches which have continued through many years. This work began with an attempt to solve the problem of surgical shock, from which it progressed further into the field of disease phenomena, and finally, into the domain of so-called "normal" processes. This study seems to have shown that the causation and origin of most normal and pathologic phenomena differ in no fundamental respect.

One result of this research has been the accumulation of evidence tending to show that in the distribution of contact ceptors, of chemical ceptors, of the mechanisms for overcoming pyogenic infections and for blood clotting; in the distribution of pain areas and of special reflexes we have a phylogenetic summary of the evolution of man.

The first practical application of these studies was the formulation of a method of prevention of shock through *anoci association*, or the absence of harmful stimuli. The principle of *anoci association* was deduced from hypotheses based upon experiments. For the key which might lead us to an explanation and further application we turned to the past history of the species. Here we found not only a satisfactory

explanation of our accumulated data, but suggestions for a further research, which has resulted in the formulation of *certain mechanistic conceptions of disease.*

Our studies showed that inhalation anesthesia does not prevent the transmission of traumatic impulses from the field of operation to the brain, and that shock is the result of the combined effect of these traumatic impulses and of pre-operative fear upon the brain. We found also that as a result of shock or exhaustion from any cause, certain histologic changes occur uniformly and constantly in certain organs — notably the brain, the liver and the adrenals, and we discovered that both the clinical and the histologic phenomena of shock could be eliminated by the prevention of pre-operative fear and by "blocking" the nerve paths from the field of operation to the brain by local anesthesia used in addition to general anesthesia. These facts having been established experimentally and clinically, a *Kinetic Theory of Shock* was formulated.

This theory accounts for shock as a natural phenomenon related to all other natural phenomena, and, like them, a manifestation of a biologic law, the *Law of Phylogenetic Association.* According to this law, animals are so constituted as to transform energy, at the incidence of an adequate stimulus, in accordance with the adaptation of the species to those factors in the environment which through natural selection have become adequate stimuli. Thus, when a barefoot boy steps upon a sharp stone, there is an instant discharge of energy in a motor act of self-preservation. This act is neither a conscious reaction, nor one due to

the boy's individual (ontogenetic) experience, but is the result of the adaptation of his progenitors, through natural selection, throughout the vast eons required to evolve the species, during which the frequent recurrence of similar mechanical injuries resulted in the implantation of a neuro-muscular mechanism, adapted to discharge automatically, at the needed moment, the required amount of energy in the form of an adaptive muscular action.

It seems probable that in like manner most, if not all reactions are performed. Every adequate stimulus awakens an ontogenetic or phylogenetic memory or *association*. This leads to *adaptive* energy transformation — an act performed. The energy thus expended is subtracted from the sum total of available potential energy stored in the body. If these stimuli be of sufficient intensity and sufficiently prolonged, the stores of potential energy are diminished, and *acute acidosis is established*, *i.e.*, the state of shock may be produced. But the discharges may be of such slight intensity and of such short duration that no appreciable diminution in potential energy is caused; in which case the responses — as in the case of the boy stepping on a stone — are deemed normal and not pathologic.

Our experiments have demonstrated that traumatic and psychic stimuli produce an increased hydrogen-ion concentration of the blood, *i.e.*, increased acidity. If the acid production exceeds the body's capacity for neutralization, there results a condition of acute acidity to which may be due in part, or perhaps entirely, the rapid respiration, the sweating, the thirst, the restlessness, which are present in shock.

Our research showed that animals subjected to *fear* without muscular activity showed the same phenomena of exhaustion and the same uniform histologic changes in the brain, the adrenals and the liver, as were shown by animals exhausted by *traumatic* injury under ether or by the *muscular exertion of running or fighting.* It is therefore obvious that these three types of exhaustion are similar, the difference being that fatigue from physical exertion results from an integration of the motor mechanism with complete response in activity or obvious work performed; while shock or exhaustion caused by emotion results from an integration of the nervous mechanism without obvious work performed. In the latter case the exhaustion is comparable to the effect produced in an electric automobile which has been integrated to go ahead by a closed circuit, while the wheels of the machine are held immobile.

Having demonstrated the apparent truth of the *Kinetic Theory* for traumatic and psychic shock, we undertook further researches to determine whether this theory explained also the exhaustion produced by infections, by drug stimulants—such as strychnin, by toxins, by foreign proteins, by insomnia, by exertion, etc. To this end we examined all the organs and tissues of animals exhausted by the bacteria and toxins of infections, by foreign proteins, by drug stimulants, by adrenin, by thyroid extract, by many other activating substances and by insomnia. The results of this study showed that as in shock, histologic changes were produced only in the brain, the adrenals and the liver and that these histologic changes were identical, whatever the cause of exhaustion. We

found also that these changes were diminished by depressing the activity of the brain by administering morphia or nitrous oxide during the application of the stimuli. In other words, the stimuli of mere consciousness and the stimuli of injury, of fear, or of infection cause these fundamental lesions; morphia and nitrous oxide diminish them; sleep cures them.

The foregoing data offer an explanation of the identical phenomena which are attendant upon certain forms of external and internal activation, but they are insufficient to explain the uniform and, to a large degree, exclusive participation of certain organs — the brain, the adrenals, the liver, the thyroid and the muscles — in the production of the phenomena. We must infer, however, that these organs bear the brunt of the transformation of potential into kinetic energy and the neutralization of the consequent acid by-products in the body and that they have been evolved for that purpose. They merit therefore the distinction of being termed the *Kinetic System.*

According to the evidence we shall present the functions which these organs are presumed to perform in the process of transforming energy are as follows: The *brain* is the initiator of response, being activated by the environment within or without the body; acting like a storage battery, it contributes the initial spark and impulse which drives the mechanism. The *adrenals* act as oxidizers, making possible the transformation of energy and the neutralization of the resulting acid products. The *liver* is the chief fabricator and storehouse of the carbohydrate fuel by which muscular action and heat are produced. The liver

also plays a large rôle in the neutralization of the acid products of the transformation of energy. The *muscles* are the engine or motor in which is consummated the final step in the transformation of energy into heat or motion. The *thyroid* by supplying a secretion which facilitates the passage of ions would seem to be the organ of speed control, governing the rate at which the transformation of energy is effected.

The postulation of the *Kinetic System* offers an explanation of the phenomena of acute activation of the organism by *infection*, by *foreign proteins*, by *exertion*, by *emotion*, and by *physical injury*. As we have already stated, our experiments have demonstrated that increased activation produces increased acidity which in turn throws increased work upon the organs by which the neutralization of acid is accomplished. As our evidence has accumulated, we have come to see that more of the chronic diseases result from the *excessive work thrown upon certain organs for the elimination of the superabundant acid products of energy transformation than result primarily from the energy transformation itself.*

The *Kinetic Theory* offers an explanation of the fact that many different diseases are apparently the outcome of the same cause, and of the equally puzzling fact that certain diseases may be the outcome of various causes. It suggests the manner in which continuous activation of the Kinetic System may cause Graves' disease, neurasthenia, cardiovascular disease, diabetes, indigestion, certain forms of acidosis and Bright's disease.

The Kinetic Theory throws light not only upon the course but upon the origin of many of the so-called

"diseases of modern environment," which are justly regarded as accompaniments of over-strenuous activity, and it suggests that these diseases are in many instances the logical outcome of causes largely within the control of the individual.

Moreover, the Kinetic Theory explains why certain therapeutic measures now in use for these diseases are remedial and suggests certain others based upon the principle of the conservation of energy through the exclusion of harmful stimuli (*anoci association*).

We shall offer evidence that the organs in the Kinetic Chain are interdependent; that the total work output of the mechanism may be increased or diminished according to the increase or diminution of the functional activity of any one link in the system. In this we have a fact of important therapeutic significance in the treatment of diseases which result from excessive kinetic activation. It was by the utilization of this principle that we perfected the shockless operation. The principle of *anoci association* was thus shown to be, in essence, an application of the principle of the *conservation of energy*, which might be utilized with equal efficacy in other conditions resulting from the overexcitation of the Kinetic System, whether by psychic, traumatic, infection, foreign protein, or drug stimulation.

We shall offer further evidence that deep opium narcosis (depression of the brain link) diminishes the transformation of energy and conserves the organs of the Kinetic System from destructive activation by traumatic injury, emotion, the injection of toxins and foreign proteins. The value of opium and of its deriva-

tives in peritonitis (the Alonzo Clark treatment) and in diabetes and arteriosclerosis has long been known. It is equally well known that the Kinetic System may be conserved in Graves' disease by depression of the thyroid link through ligation of the arteries or excision of a portion of the gland. We shall attempt to show that, in like manner, certain other chronic diseases which are temporarily improved by morphia may, like Graves' disease, be permanently improved by a surgical modification of the Kinetic System.

As we have stated, emotional activation — activation by worry and fear particularly — is as potent in causing excessive transformation of energy and an excessive production of acid by-products with consequent physical impairment as are any other kinetic stimuli. It is obvious, therefore, that the absence of worry and fear may aid in stopping the body-wide activations which lead to an organic breakdown. The therapeutic value of rest, of change of scene, of diversion, and the restorative powers of happiness and success and congenial surroundings are thus explained in terms of approximate physical value.

The significance of the principle of energy conservation to many phases of life is no less impressive. If the effect upon physiological processes of faith in the remedial agent is of itself far-reaching, to what extent might not the conservation of energy accomplished as a result of education and training, of a larger knowledge of natural laws and true values in life, aid in the attainment of a happier adaptation to environment.

It is particularly in the domain of preventive medicine, however, that the application of the mechanistic

principle of the conservation of energy in the human body is of immediate and practical benefit. That faith in a final outcome for good can control and may even prevent the occurrence of many abnormal states which border closely on disease, we have abundant proof. That it can be utilized to a far greater extent than is now realized is the indication of our findings in the laboratory and in the clinic. To what extent it may be utilized scientifically depends upon the disclosures of further research. Perhaps an indulgent hearing may be invoked for the author's belief that the individual who accepts the theory of the conservation of energy in the Kinetic System can and undoubtedly will do much to stem the tide of harmful activities now draining his energies to no purpose; and that with this clearer understanding he will be able to construct for himself a plan of life more conducive to longevity and happiness than his present blind yielding to environmental coercion.

It is with the desire of increasing the scope of preventive medicine; with the hope of relieving and even of curing certain acute and chronic diseases and of stimulating a biologic trend of thought in medicine to the end that disease like health may be given its evolutionary setting, that this volume is offered.

PART I

GENERAL CONSIDERATION OF BIOLOGIC ADAPTATION AND ASCENT OF MAN

CHAPTER I

ADAPTATION TO ENVIRONMENT

Everything in nature, living or not living, exists and develops at the expense of some other thing, living or not living. The plant borrows from the soil; the soil from the rocks and the atmosphere; men and animals take from the plants and from each other the elements which they in death return to the soil, the atmosphere and the plants. Year after year, century after century, eon after eon, the mighty, immeasurable, ceaseless round of elements goes on, in the stupendous process of chemical change, which marks the eternal life of matter. No human imagination is powerful enough to picture the vast, the infinite antiquity of the tiniest particle of matter which composes our present bodies and environment, or the varied and spectacular trail of cosmic vicissitudes through which it has passed.

To the superficial observer, nature in all her parts seems imbued with a spirit of profound peace and harmony; to the scientist it is obvious that every infinitesimal particle of the immense concourse is in a state of desperate and ceaseless struggle to obtain such share of the available supply of matter and energy as will suffice to maintain its present ephemeral form in a state of equilibrium with its surroundings. Not only is this struggle manifest among living forms,

among birds and beasts and insects in their competition for food and habitat, but — if we may believe the revelations of the science of radio-activity — a process of transmutation, of disintegration of the atoms of one element with simultaneous formation of another element, is taking place in every fragment of inanimate matter, a process which parallels in character the more transitory processes of life and death in organisms and is probably a representation of the primary steps in that great process of evolution by which all terrestrial forms, organic and inorganic, have been evolved from the original ether, by an action inconceivably slow, continuous and admitting of no break in the series from inanimate to animate forms.

By the superficial observer only two kinds of phenomena are distinguished in nature, the living and the non-living; animate and inanimate matter; but to the scientist nothing is dead. All matter participates in the universal inter-atomic whirl, of which radio-activity is a marvelous manifestation, and within the atom there are worlds within worlds of concentrically moving particles. The universe is a seething caldron of continuous change, the basis of which is motion. Motion underlies all change, whether physical or chemical, in both animate and inanimate matter. Growth and decay are but relative changes which express the common tendency of all cosmic forces to equilibrium.

The Coming of Life

What initiated motion, science cannot tell us. In the main, however, scientists agree in regarding the

process of evolution as continuous from the birth of the earth in star nebulæ to the coming of man, although it is unknown how many and how varied have been the steps between, or how infinitely prolonged has been the process. We know that vast periods of time must have intervened between the inauguration of motion and the appearance of forms approximating our terrestrial rocks and gulfs; and that additional myriads of ages must have been required to produce the first ultramicroscopic particles of *quasi*-living matter, which scientists regard as the probable step intermediate between non-living and living matter. How many more millenniums had to pass before undoubted moving, assimilating and reproducing forms of life appeared, it is useless to conjecture. It is probable, however, that the terrestrial stage was already well stocked with reactionary factors in the shape of gases, liquids, solids, light, changing temperatures, and the like, when the first mass of ancestral colloidal slime appeared.

From colloidal slime to man is a long road, the conception of which taxes our imaginations to the utmost, but it is an ascent which is now fairly well demonstrated. Indeed, the problems of the missing links are not so difficult as is the problem of the origin of the organs and functions which man has acquired as products of adaptation. For whether we look upon the component parts of our present bodies as useful or useless mechanisms, we must regard them as the result of age-long conflicts between environmental forces and organisms.

As a result of the struggles for survival, there ensued automatically an approximate adjustment of indi-

viduals to the supply of food, which has resulted in the present almost perfectly balanced distribution of groups and species of plants and animals, all utilizing in cycles the same matter and the same energy. Plants obtain their nourishment from mineral substances through their utilization of solar energy. Plants are food for animals; animals die, disintegrate and become food for plants. Thus matter circulates eternally, the radiant energy of the sun being transformed by plants into chemical energy, which in turn supplies the energy of animals, by which it is returned to the external world in the form of heat and motion. All this is accomplished in such a way and in such succession as to occasion the least amount of friction, so as to give, indeed, an effect of perfect harmony throughout nature.

In all this concourse of living and non-living bodies, the one most conspicuous feature is the facility with which each individual — atom, molecule, animal, species, group — responds in an adaptive manner to the entities in its environment, or dies — disintegrates — and in disintegrating surrenders the elements which allow other entities to assume the burden of existence or to become more completely adapted to their surroundings. It is the omnipresent working of this universal law of equilibrium, compromise, or "adaptation," which is at the bottom of that appearance of homogeneity and peace which leads the casual observer to believe that nature is the result of design. The peace he sees, however, is but the relative peace of the center of a mighty whirlpool, or the grim, trenchant peace of the battle-field deserted after carnage; and

the harmony is but the harmony of gigantic wheels driving round in perfect rhythm, but, as they drive, grinding like the "mills of the gods, exceeding small and most exceeding fine."

The Struggle for Existence

Darwin has called this process of friction and change in nature the "struggle for existence." He shows, in the "Origin of Species," how this struggle results in the "elimination" of types "unfitted" to survive, and in the perpetuation of types in all respects "fitted to survive" because their forms and functions have been fashioned by adaptation. For the sake of convenience and vividness we retain most of the familiar terms of Darwin. But it is not strictly in accordance with the mechanistic view, which we hold, to speak of an automatic reaction as a "struggle" between the reagents. One does not assume struggle or volition on the part of the elements when they enter into chemical combination. In like manner, although it is convenient to speak of this world-wide activation, which destroys many that a few may survive, in terms of the struggle which it resembles, we do not assume the existence of any "innate faculty" or "will" or "desire to live," either in the individuals which survive or in those which are lost. Many terms of the established vocabulary of evolution have a tendency to convey this teleological meaning, which we wish to avoid. For that reason, whenever in the description of natural processes it is possible to substitute a word or phrase equally brief but more neutral than the old terms, we shall do so, avoiding the phraseology, while main-

taining the principle of evolution. From this viewpoint the operations of "natural selection" are passive rather than active; are portrayed in terms of both environment and species, rather than in terms of species alone.

Mechanisms of Adaptation

In the first delight of finding a rich display of beautiful and ingenious mechanisms for the preservation of life in plants and animals, we are prone to overestimate the "marvelous efficacy" of these contrivances, and to ignore the presence of many imperfect and involved mechanisms, which make life precarious for the average organism. For example, what a vast amount of superfluous energy has apparently been wasted in making the long-distance arrangements for fertilization in certain plants, which first produce flowers and then the nectar by which to attract insects on the chance that they may brush against the pollen and carry it to another flower! How crude are some of the mechanisms in human bodies — the twenty or more feet of intestines, which give harborage to poisonous germs and gases; the *appendix vermiformis*, and various other cumbersome arrangements, which the surgeon is daily called upon to remedy!

The fact is that the present form of man is the result of an inconceivably long and tedious process of addition and subtraction, of grafting character upon character in somewhat the same haphazard fashion as in certain mountains in South America stones are thrown by the wayfarer upon a lone Indian grave. Some land se-

curely and augment the mound, while others fall at random and roll away, the desired result being achieved, however — a memorial to the one who lies beneath the pile. If the result of man's haphazard assemblage of organs is to some extent adequate to the needs of his present environment, it is because during the age-long processes of evolution all the fatally awkward combinations have been eliminated by a struggle so keen that the slightest variation in the length of a leaf, the strength of a limb or the color of an egg, has given the victory to a rival species. Throughout this struggle survival has depended on one of two conditions: the possession of extreme *stability*, the quality of withstanding all destructive forces in the environment; or the possession of *lability*, the quality of adaptability to various conditions in the environment. Rocks are an example of the first condition; man and higher animals of the second.

Twenty-four hundred years ago Heraclitus likened life to a flame, and no analogy more fitting has ever been proposed. Life is sustained by the same sort of combustion as that in the flame. The contour of the flame, like the outward aspect of the body, is ever the same, but the contents of both are continually changing. In the flame atoms of carbon and of oxygen are constantly combined to form carbon dioxid and energy is constantly released in the form of heat, while in the body energy is derived from the oxidation of carbon contained in foodstuffs. Like the energy in coal the energy latent in food compounds was obtained originally from the sun. The energy-containing food compounds in plants are devoured by plant-eating animals,

and again by flesh-eating animals, which prey upon the herbivora. In their bodies it is reduced again to carbon dioxid and exhaled, only to be reabsorbed again by plants, stored again in plants by sunlight and again taken into the animal body. Thus occurs the ceaseless round of matter and energy, by which is perpetuated a complete cycle of "adaptation," not only of plants and animals to each other, but of elements to organisms, and of all to the sun's radiance.

As we rise higher in the life scale, the law of "adaptation," by which character is silently and invisibly determined in the world of atoms, becomes more obvious and concrete, until in the world of animals it is exemplified by a face-to-face conflict of individuals which is more desperate and thrilling than any artificial drama ever staged by man. Here in a world-wide trail of blood are to be traced the workings of that invisible law of balance, the violation of which among gases meant only "friction." On land and sea, in forest, field and stream, are to be seen evidences of the mighty conflict resulting in the elimination of those individuals unfit for survival, and the perpetuation of species safely modified to their surroundings. In looking out upon the face of nature, radiant with sunshine, color and the song of birds, it is hard to believe that a wholesale destruction of life is being enacted in every corner of verdant splendor. Yet each one of those little birds singing so blithely, each of the skipping grasshoppers, has made a meal of some other living thing in its environment. In the downward swoop of the robin upon the worm, in the hasty scamper of a rabbit through the fern, in the steady pecking of the wood-

pecker for insects in the bark of a tree, in the lightning-like dash of a lizard to cover under a rock, in the stealthy advance of a snake upon a bird's nest, in the scream of an eagle overhead, we have vivid glimpses of nature showing her teeth, of the tragic side of life, which, because it is familiar to us, seems right and beautiful and placid.

Everywhere something is pursuing and something is escaping another creature. It is a constant drama of getting food and of seeking to escape being made food, evolving in the conflict structures fitted to accomplish both reactions. Everywhere the strong prey upon the weak, the swift upon the slow, the clever upon the stupid; and the weak, the slow, the stupid retaliate by evolving mechanisms of defense, which more or less adequately repel or render futile the oppressor's attack. For each must live, and those already living have proved their right to existence by a more or less complete adaptation to their environment. The result of this twofold conflict between living beings is to evolve the manifold structures and functions — teeth, claws, skin, color, fur, feathers, horns, tusks, wily instincts, strength, stealth, deceit and humility — which make up character in the animal world. According to the nature and number of each being's enemies has its own special mechanism been evolved, distinguishing it from its fellows and enabling it to get a living in its particular environment.

The survival of any organism implies that it is protected against adverse climate, against starvation and against annihilation by enemies, in order that it may live and produce offspring. In each instance,

the conditions governing the struggle vary, and the evolved mechanisms are correspondingly distinctive. In the waste places of the earth the struggle is more particularly with the climate — against the severity of heat, cold and drouth, and against a scarcity of food. Here may be seen such devices as are found among the plants of the desert — gaunt, geometrical forms covered with spikes instead of leaves, to prevent the evaporation of moisture, and with roots which are many times the size of the bush above, that they may make vast ramifications into the earth below in a search for water. Again, in more verdant spots, where food is plentiful, but many individuals are seeking it, the fight for possession is between species as well as within each species. Here the plant, supplied with abundant moisture but surrounded by a thicket of other equally eager plants, must evolve a device for scattering its seeds abroad. Hence come the various contrivances of fruit and flowers by which animals are enticed to devour the seed and eject it; or by which the seeds are easily disseminated by the wind — balloon-like pods in which the seeds are encased, easily rolled along by the wind; hooks or spikes by means of which the seeds adhere to the hides of beasts; or elegant plumage like that of the dandelion, by means of which the seeds are lightly wafted by the breeze. Each variation, as it occurs sporadically, is adjudged by the environment, condemned and suppressed if harmful; approved, perpetuated and perfected if advantageous.

The same end is attained by a variety of means, each organism seeming to have hit upon a combina-

tion not preëmpted by others and coming finally to depend upon its one particular mode of defense. Here, a weak, stupid animal is sheltered under a shell or carapace, leading its narrow life in the very shadow of fierce and powerful animals, yet effectively protected from them. Here, another flits from limb to limb lightly, pecking its food daintily, hiding its eggs carefully, and skillfully deceiving or diverting its wily and more powerful enemies. Here, a sleek and lazy creature, without shell or armor, wings for flying, or claws for fighting, keeps its enemies at a distance by the production of an acrid or repellent odor. Here a slipping, sliding thing effects by fangs and venom what its neighbor accomplishes by a barbed skin or a repulsive emanation. Here, a huge forest prowler, muscled as with whipcord, survives by sheer strength, while another, lacking this strength, depends upon the fleetness of its limbs, the keenness of its eye, the acuteness of its hearing, living on its wits as verily as any human adventurer. Here, a delicate little creature, like the field mouse, preyed upon by everything in its neighborhood — snake, hawk and owl, lacking any of the more powerful defenses, survives by the sheer fact of its great fertility. Here, the elephant, slowest of breeders, being superior to attack, stalks unmolested through the forest, but finds its struggle in a hunt for food.

In every case the fate of each creature seems to have been staked upon one mechanism. The tiger by its teeth and claws, the elephant and the rhinoceros by their strength, the bird by its wings, the deer by its fleetness, the turtle by its carapace — all are enabled

to counter the attacks of enemies and to procreate. Where there is a negative defense, such as a shell or quills, there is little need and no evidence of intelligence; where a rank odor, no need and no presence of claws or carapace; where sting or venom, no need and no possession of odor, claws, shell, extraordinary strength or sagacity.

Where the struggle is most bitter, there exist the most complex and most numerous contrivances for living. Where food is easy of access, as, for instance, among some sea animals which feed upon the microörganisms in the water, there is little need of more than the siphon-like appendages which are waved about in the medium containing food while the animal like a plant clings to a rock or shell.

Form and Color Obliteration

Obliteration of color and form is one of the most effectual methods by which certain animals survive. So useful has been this device of color obliteration that in practically every part of the world many living things are in color similar to the immobile things among which they live. Thus green is a common color for animals in the evergreen forests of the tropics; white is the prevailing color in the arctic regions and a yellowish hue is common in desert places. Some birds, like the ptarmigan, an inhabitant of the Canadian Rockies, alter their color according to the season of the year to match colors in the environment, their coats being white in the winter, green or gray in the summer and mottled in the spring and fall. (Fig. 1.) The ermine fox of the north has the

FIG. 1. — PROTECTIVE COLORATION OF THE ROCKY MOUNTAIN WHITE-TAILED PTARMIGAN.

same adaptability. Creatures that commonly haunt the night, such as mice, moles and bats, have a dusky hue. The fishes that swim along the coral reefs in tropical waters have gorgeous tints which mingle with their environment. Certain marine organisms that float on the surface of the water are tinged to accord with the scenery above and below their habitat, so that from above they appear blue, in harmony with the color of the ocean, while to their enemies below they are white, harmonizing with the clouds and the foam as seen from below.

Many animals, conspicuous when they are out of their native haunts, are practically invisible in their natural habitats. The vividly striped zebra, and the tiger with its yellow and black markings, when seen in the midst of the tall grasses and reeds of their natural environments are so identically a part of the light and shadows as to be scarcely noticeable. The giraffe, with its knotty head and blotchy skin, when standing in the thickets of its native forest, is a perfect match for the blanched and broken branches of dead trees.

Among the small creatures of our own forests and plains, concealing and revealing coloration is a constant source of surprise and interest to the beholder. It is not its coloring alone but also its shape and its manner of holding itself in relation to the object upon which it rests, that secures for an animal the resemblance which is its protection against enemies which are often of similar color and shape. Down in a cool spot near a stream in the woods one may see a green frog poised for a fly, the fly so colored as to be scarcely visible over the surface of the water, while above hangs

a brown-and-green snake, head extended, fangs out, ready to pounce upon its green victim, the frog; behind the snake and above it, the almost invisible snake-eating bird is poised for her prey with the same calm assurance that she herself is unseen. Sometimes the protective coloring extends only to the offspring or to the eggs, which are colored so as to match the leaves among which they lie. The little chicks of the wild turkey, herself more or less protectively colored, are perfectly matched to the dry yellow leaves among which lies the nest, from which the mother turkey may depart and leave them in security.

As we thus look out upon the vast array of life, we see species that have made use of every possible opportunity open to them. What one has not found as a mode of defense, another seems to have hit upon with a marvelous aptitude. Every form of diet, every phase of environment, every device for capture or escape has apparently been utilized.

Throughout its whole course the process of evolution, where it is visible in the struggle of organisms, has been marked by a progressive victory of brain over brawn. And this, in turn, may be regarded as but a manifestation of the process of survival by *lability* rather than by *stability*. Everywhere the organism that exhibits the qualities of quick response, of extreme sensibility to stimuli, of capacity to change, is the individual that survives, "conquers," "advances." The quality most useful in nature, from the point of view of the domination of a wider environment, is the quality of *changeableness, plasticity, mobility* or *versatility*. Man's particular means of adapta-

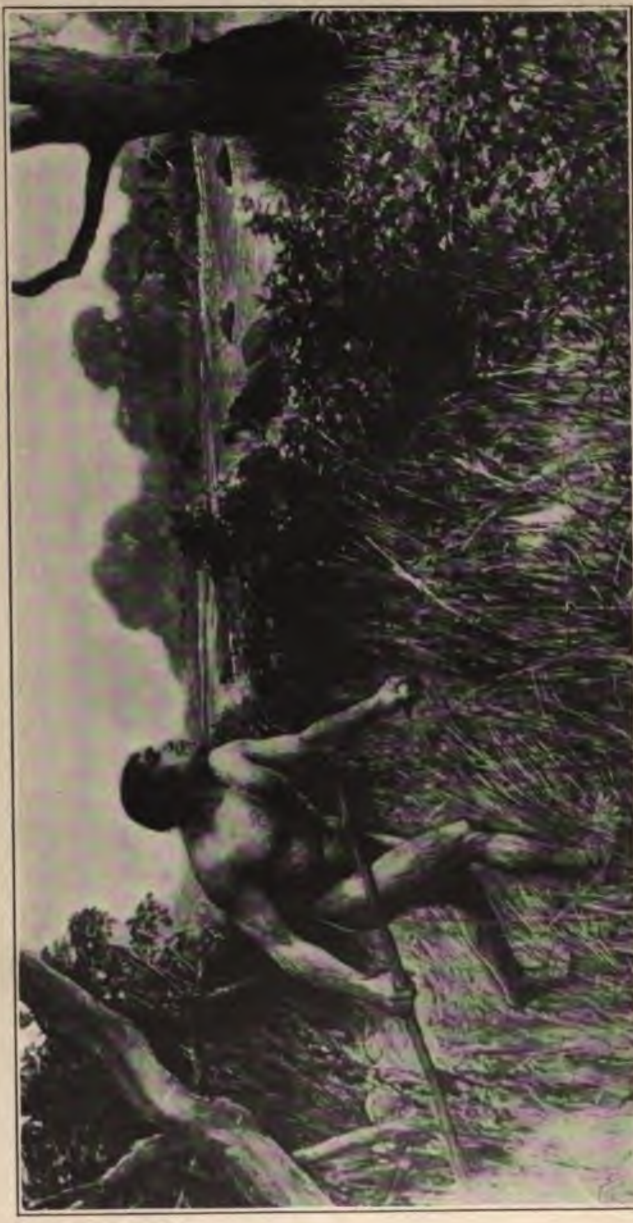
tion to his environment is this quality of versatility. By means of this quality expressed through the manifold reactions of his highly organized central nervous system, man has been able to dominate the beasts, and to maintain himself in an environment many times more extensive than theirs. Like the defensive mechanisms of shells, poisons and odors, man's particular defensive mechanism — his versatility of nervous response (mind) — was acquired automatically as the result of a particular combination of circumstances in his environment.

The Rise of Man

In the Tertiary era — some twenty millions of years ago — the earth, basking in the warmth of a tropical climate, had produced a luxuriant vegetation, and a swarming progeny of gigantic small-brained animals for which the exuberant vegetation provided abundant and easily acquired sustenance. They were a breed of huge, clumsy and grotesque monsters, vast in bulk and strength, but of little intelligence, that wandered heavily on the land and gorged lazily on the abundant food at hand. At that time there prevailed such types as the giant dinosaurs, mere feeding and breeding machines. They were essentially the product of prosperous days, destined to perish at the first onslaught of adversity. With the advance of the carnivora, the primitive forerunners of our tigers, wolves, hyenas and foxes, came a period of stress, comparable to a seven years of famine following a seven years of plenty, which subjected the stolid herbivorous monsters to a severe selective struggle.

Before the active onslaught of lighter, lither, more intelligent foes, the clumsy, inelastic types succumbed, those only surviving which, through the fortunate possession of more varied reactions, were able to evolve modes of defense equal to the modes of attack possessed by their enemies. This was a time when the quality most needed for survival was the ability to perceive enemies afar and to flee from them. The majority of the leaf-eating species could not stand this test and perished. Those more plastic forms which survived became our modern horse, deer, antelope, ox and elephant. Many, unable to evolve the acute senses and fleet limbs necessary for the combat on the ground, shrank from the fray and acquired more negative and passive means of defense. Some, like the bat, escaped into the air. Others, such as the squirrel and the ape, took refuge in the trees.

It was in this concourse of weak creatures which fled to the trees because they lacked adequate means of offense, defense or escape on the ground, that the lineaments of man's ancient ancestor might have been discerned. One can imagine what must have been the pressure from the carnivora that forced a selective transformation of the feet of the progenitor of the anthropoids into grasping hands. Coincidentally with the tree life, man's special line of adaptation — *versatility* — was undoubtedly rapidly evolved. Increased versatility and the evolution of hands enabled man to come down from the trees, millions of years thereafter, to conquer the world by the further evolution and exercise of his organ of strategy — the brain. Thus we may suppose have arisen the intri-



From the Illustrated London News.

FIG. 2. — THE SUSSEX MAN.

The most ancient known inhabitant of England. Reconstructed from the jaw and a portion of the skull of a skeleton found by Mr. Charles Dawson in Uckfield, Sussex, England, in 1912.

cate reactions we now call mind, reason, foresight, invention, etc.

In the end it proved unfortunate for the carnivora that they forced the ancestors of man to the trees, for it was there that they secured the training which made it possible for primeval man to wage upon the carnivora a warfare a thousand-fold more disastrous than the latter had waged upon the stupid Tertiary monsters. With what bewilderment these autocrats of the forest must have viewed the maneuverings of these little beasts, which they had learned to disregard because of their lack of strength or weapons, as they prepared a defense out of sticks and stones! With what amazement they must have watched these primeval men as they fled to the hills and sent back stinging darts and flint-tipped arrows that bit into the flesh and clung and brought them low! (Fig. 2.) With what awe they must have peered out upon the first ring of fire man built for himself as a protection against their marauding; and how strange and halting must have been the first faint gropings of man himself in the use of that mighty element, mastery over which was to mean to him the lordship of all creation! No pen is powerful enough to depict the thrilling details of this most wonderful of all stories — the tale of man's gradual rise, of the age-long conflict, marked by desperate hand-to-hand encounters, by wild flights through the brush, by cautious reconnoiters, by sudden sorties and renewals of the battle which was to end in death or victory. No wonder that memories of the wounds and hazards of the conflict have been implanted deep within us and are manifested in overpowering fear of

certain animals, colors and noises, and in sensations of pain when we are cut or struck. No wonder that the fear and respect aroused by the brute courage and strength, which were acquired in the flesh-to-flesh encounter, survive to-day in the savage's acceptance of the brute as a social equal; in the Veda religions; in the ceremonials of animal worship; in some countries in edicts against the slaughter of animals; in the ancient art which depicted man as half man, half beast; and in many other phases of ancient and modern civilization. The sense of the close relationship of man to the brute world is the essence of Totemism, that peculiar system of superstition by which the Alaskan Indian proclaims his mystic union with ancestral groups of plants and animals.

Modern life, indeed, abounds in evidences of the "mark of the beast" and any effort to reconstruct the story of the past conflict leads to a recognition of the fact that the story is still in the telling. There has been no halt in the steady progress of the fray, and man is still a changing, modifiable organism, — is still through selection being adapted to surrounding nature by means of the mechanism which secured to him sustenance and safety in the past and now secures to him safety from bacterial, brute and human menace. With changes in environment have come changes in the conditions governing the contest, and corresponding alterations in man's chief mechanism of adaptation — the brain. The enemy without the clan has been succeeded by the enemy *within* the clan, and clan life itself, first used as a defense, has brought its own quota of difficulties for the adjustment of which there

have been evolved reactions more delicate, more subtle and more complex than were needed in man's primitive existence. The evolved mechanism by which man responds to the new elements in his environment by processes of reason, invention, sentiment, moral precept, laws, customs and social organization, may seem vastly more "elevated" and abstract than the reactions of digestion, locomotion and "instinct," which suffice for the "lower" orders. The mechanism by which the more complex reactions are brought about, however, is similar to that which, in its earliest form as a group of specialized cells, coördinated the movements of the *Amphioxus* for purposes of locomotion and digestion; in a later form as the simple brain of the struggling vertebrates, gave acuteness of sight and fleetness of limb to the tree-climbing species; and, as the brain of the caveman, contributed ability to fashion and to fling his arrow weapons.

"Mind," the word we use to express the reactions of this mechanism, is no phenomenon apart and distinct from other functions of the nervous system. Indeed, mind, as we find it in the "lower walks" of life, is not confined to animals. Many plants exhibit in response to external stimuli protective reflexes which are analogous to the nervous reflexes of man. Notable among these are the drooping of the leaves of the sensitive plant when it is lightly touched, and the movements by which the *Drosera* and Venus' flytrap capture and digest their prey when they are excited by the touch of an insect. It appears that sensitiveness to stimuli, which is the first form of mind, has been distributed in organisms, coincidentally with

mobility. To stationary plants, except in the case of the insectivorous forms, such irritability could be of little benefit to the species; but to the pursuing and pursued organisms it is of great advantage. In his treatise on climbing plants Darwin remarks that it has sometimes been asserted that plants are distinguished from animals by their lack of power of motion, and he succinctly adds: "It should rather be said that plants acquire and display this power only where it is of some advantage to them."

The test of utility may be applied to internal processes as well as to external manifestations in custom and social forms of man's peculiar mode of adaptation by nervous reactions. On this basis man's claim to a superior place among animals depends less upon *different reactions* than upon a *greater number* of reactions as compared with the reactions of "lower" animals. Ability to respond adaptively to more elements in the environment gives a larger dominion, that is all.

The same measure applies within the human species, — the number of nervous reactions of the artist, the financier, the statesman, the scientist, being invariably greater than the reactions of the stolid savage. That man alone of all animals should have achieved the degree of versatility sufficient for such advance is no more remarkable than that the elephant should have evolved a larger trunk and tusks than the boar; that the legs of the deer should be fleeter than those of the ox; that the wings of the swallow should outfly those of the bat. Each organism, in evolving the combination of characters commensurate with safety in its

particular environment, has touched the limit of both its necessity and its power to "advance." There exists abundant and reliable evidence of the fact that wherever man has been subjected to the stunting influences of an unchanging environment fairly favorable to life, he has shown no more disposition to progress than the most stolid animals. Indeed, he has usually retrograded. The need to fight for food and home has been the spur that has ever driven man forward to establish the manifold forms of physical and mental life which make up human existence to-day. Like the simple adaptive mechanisms of the plant, by which it gets air, and of the animal, by which it overcomes its rivals in battle, the supremely differentiated functions of thought and human relations are the outcome of the necessity of the organism to become adapted to entities in its environment, and are best explained by a study of the details of this relationship.

PART II

THE MECHANISMS OF ADAPTATION: RECEPTOR AND EFFECTOR

CHAPTER II

THE NERVOUS SYSTEM

One of the most unfortunate heritages bequeathed to man by the age-long conflict with brute creation is an intellectual timidity, a reluctance to look upon natural phenomena from the point of view that the conditions of life itself are the impelling, determining forces in evolution. Man is prone to deprecate natural processes and appetites as base; to deplore the "utilitarian" in life and in philosophy; and to account for vital manifestations on the ground of an extraneous supernatural will. Undoubtedly this tendency is a relic of a long period of bodily persecution, of dread of superior foes, during which, by superstitious worship, by sacrifice and by pretending to despise life, men sought to enlist the protection or to divert the interest of unseen superiors. Galton has shown that timidity and lack of self-confidence are qualities common to all animals of gregarious habits, in which, because of their advantage to herd life, these characters have been developed and perpetuated by natural selection. He shows also that these same instincts in man, his lack of independence, and his subservience to tradition, authority and custom are the result of enforced subjection to the will of the clan, during the long period of adaptation through social coördination.

With the acceptance of the theory of evolution, however, has fallen the last barrier to an impersonal

consideration of the body. It is now as reasonable to explain a muscular reflex or an internal secretion by its utility in the life of the organism, as to explain the webbed foot of an amphibian or the teeth of a carnivore on the same basis.

In like manner those functions which have been arbitrarily classified as "physical," "mental," "moral" and "social" have been created by factors in the environment during the struggle for existence. In order to apply this viewpoint to the adaptive processes of man, it is necessary to divest the organism of all powers of action save that of response to stimuli, and to regard every vital manifestation in which man is directly or remotely concerned as but one phase of the organism's adjustment to environment by means of the transformation of energy in response to physical stimuli. On this basis a physiological process is an evoked phenomenon, dependent for its manifestation upon the impingement of some specific form of energy in the internal or the external environment. According to the law of conservation, this transmitted energy produces its own equivalent in a new form, which in turn may affect other forms and forces in the environment. Man is thus essentially a transformer of energy which is derived from the environment and ultimately is returned to the environment.

The reactions which compose the life of man and of other organisms are the result of the inevitable effects produced in a sensitive structure by an activating environment. In other words, the life processes of any organism depend upon the evolved mechanism by which it reacts "adaptively."

Man's special mechanism of adaptation to environment is his nervous system, which coördinates each part of the body with every other part by means of the brain, the spinal cord and a labyrinthian network of nerve fibers and peripheral nerve-endings. Recent developments in the sciences of biology, physics, chemistry and physiology suggest that this nerve mechanism is merely a highly specialized pathway for the transmission of impulses set up by environmental stimuli. In higher beings these impulses meet and coördinate, or impinge and interfere in a central organ of the mechanism, the brain, where schemes or patterns of action are formed automatically according to the lines of least resistance which have been established by the evolution of the organism and the species.

A Specialized Pathway for Stimuli

The response to external stimuli by adaptive reaction is not limited to animals endowed with a nervous system, but is common to all living protoplasm. For example, unicellular organisms respond to the stimuli in their environment by moving toward food and away from danger, these actions being paralleled by the manner in which many of the component cells in pluricellular organisms respond to stimuli. In the intestines of certain animals the cells throw out separate prolongations of protoplasm which, like the pseudopodia of amœbæ, seize minute drops of fatty matter and draw them within the main body mass.

Thus in their search for food and in other activities, the free-living protozoa furnish examples of adaptive

reactions essentially similar to the adaptive reactions of cells in the bodies of multicellular animals. A closer parallel, however, may be seen in the history of the sexual elements during the process of fertilization. The male and female reproductive elements differ in form, the ovum being usually spherical, while the spermatozoön is generally smaller and has a rounded "head" and a greatly attenuated "tail." A functional dissimilarity corresponds to this difference in form. The male element, the spermatozoön, is motile, and by the lashings of its whiplike "tail" is enabled to approach the non-motile ovum. In all probability this phenomenon is in some cases largely due to the chemotactic attraction of the sperm, though in other instances the spermatozoa cease their swimming movements when they come in contact with a smooth surface (stereotropism). The behavior of the spermatozoön is closely comparable with that of many protozoa.

Thus in nature processes are repeated many times and usually by the same pattern. In the very lowest forms of life which are devoid of any visible nervous system or other specialized tissue, are manifested reactions, which, in the higher organisms, are effected by the activities of some specialized structure, such as the central nervous system.

If, as we have intimated, this power of adaptive response is a general function of protoplasm and if "adaptive responses" constitute the sum total of "mind" and "nervous reaction," we may well ask of what use is a central nervous system in the life of higher organisms; and whether, in organisms which

have this specialized structure, adaptive response is a function of that structure only. Illumination on this point is found in the experiments made by Loeb upon the heliotropic reactions of plants and animals and on the sustained reflexes of animals whose central nervous system has been removed. Loeb showed that the phenomenon of heliotropism, that is, of orientation with respect to light, which in animals was formerly attributed to a "psychic" faculty, is essentially identi-

From Loeb's "The Mechanistic Conception of Life."

FIG. 3. — POSITIVE HELIOTROPISM OF A MARINE WORM (SPIROGRAPHIS).

"The light fell into the aquarium from one side only and the worms all bent their heads toward the source of light, as the stems of positively heliotropic plants would do under the same conditions."

cal in both plants and animals and that it occurs in both in accordance with the laws of photochemical action. (Fig. 3.) The fact that some animals exhibiting this reaction have a true central nervous system while plants have none is aside from the problem. Other animals having a diffuse type of nervous system, but no central organ, also show typical phototropism (Crozier).

If it be true, as these experiments seemed to show,

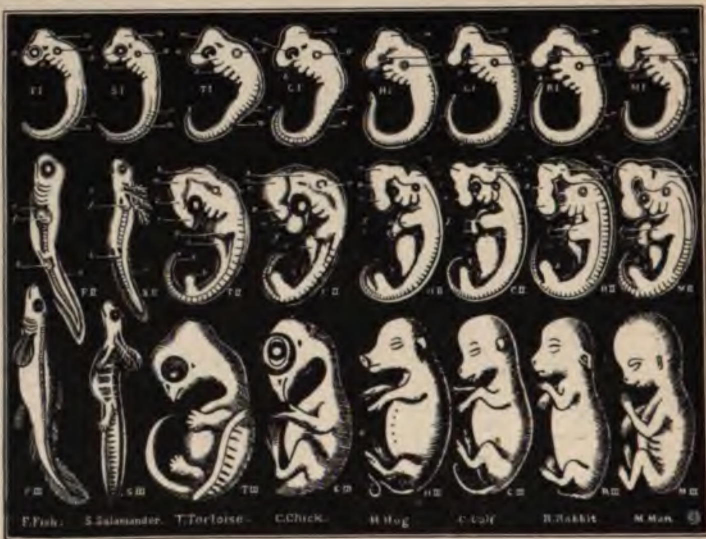
that a central nervous system is not necessary for the production of coördinated reflexes in an animal, then, it was argued, it should be possible to obtain the same coördinated reflex in an animal whose central nervous system had been removed, provided a continuous pathway of protoplasm could be maintained for the conduction of the exciting impulse from the skin to the muscles. To prove this point the central nervous system was excised from earthworms and from ascidians (Loeb). Excision of the central nervous system in these animals did not destroy their characteristic reflexes, but the crux of the situation was disclosed in the fact that, although the response of the mutilated animal to stimulation was the same as that of the normal animal, *it required more stimulation to produce response in the former, and the response was much more retarded than in the normal animal.* In other words the *threshold of stimulation* had been raised by the destruction of the specialized pathway over which the exciting impulse was accustomed to travel. The central nervous system was thus shown to be a quick and sensitive conductor by means of which the efficiency of the whole mechanism was increased. The evolution of specialized tissue is responsible for the attainment of efficiency, for as we ascend the animal scale we find that *pari passu* with the increasing differentiation and development of certain tissues, the environment dominated by the organism is widened.

Thus as we progress from the simple protozoön to the complex pluricellular organism we find evolved progressively more effectual organs of locomotion and special sense; more complicated systems of nutrition,

of circulation, of respiration, of propagation, all coördinated and controlled by a correspondingly increased mass of nervous tissue — which finds its highest development in a *brain*, wherein each kind of impulse forms its own pattern, the stimulation of which results in a specific reaction of the organism, these resultant reactions varying from the simplest motor response to the most complex process of "reason."

The age-long process by which evolution develops complex from simple mechanisms is strikingly illustrated by the embryology of the individual. In the development of the adult from the ovum there is reproduced in brief the evolution of the higher organism from the single cell. In the early human embryo appears the first rudiment of a nervous system which is of the same form as that found in larval *Ascidians*, — namely, a series of ganglion cells which coördinate reflexes for separate segments of the body. Together with the simultaneous development of the whole embryo there develops a spinal tube like that which is found in the *Amphioxus*, the lowest of chordates. At a later period, a brain develops by the enlargement of the anterior extremity of this spinal cord. At first this brain is of simple structure, like the brain of the lowest forms of fish. Gradually this simple brain develops into the more highly differentiated human brain passing consecutively through stages which in general represent the brains of the lower animal types through which man was evolved. (Fig. 4.)

The evidence strongly supports the belief that it is by no quality exclusive to itself and alien to other protoplasm that the nervous system performs its special



From Haeckel's "Evolution of Man."

FIG. 4. — COMPARISON OF THE EMBRYOS OF MAN AND OTHER VERTEBRATES.

These pictures are meant to represent the more or less complete agreement, as regards the most important relations of form, between the embryo of Man and the embryos of other Vertebrates in early stages of individual development. This agreement is the more complete, the earlier the period at which the human embryo is compared with the embryos of other Vertebrates. It is retained longer, the more nearly related in descent the respective matured animals are — corresponding to the "law of the ontogenetic connection of systematically related forms." . . .

"The first, or upper cross-row, I, represents a very early stage, with gill-openings, and without limbs. The second (middle) cross-row, II, shows a somewhat later stage, with the first rudiments of limbs, while the gill-openings are yet retained. The third (lowest) cross-row, III, shows a still later stage, with the limbs more developed and the gill-openings lost. The membranes and appendages of the embryonic body (the amnion, yelk-sac, allantois) are omitted. The whole twenty-four figures are slightly magnified, the upper ones more than the lower. To facilitate the comparison, they are all reduced to nearly the same size in the cuts. All the embryos are seen from the left side; the head extremity is above, the tail extremity below; the arched back turned to the right. The letters indicate the same parts in all the twenty-four figures, namely: *v*, fore-brain; *zz*, twixt-brain; *m*, mid-brain; *h*, hind-brain; *n*, after-brain; *r*, spinal marrow; *e*, nose; *a*, eye; *o*, ear; *k*, gill-arches; *g*, heart; *w*, vertebral column; *f*, fore-limbs; *b*, hind-limbs; *s*, tail."

function of coördinating body processes. Through evolution the nervous system has acquired certain specific qualities, which are, for nerve fibers, that of facilitating the conduction of impulses; for nerve cells, that of holding energy which may be released by nerve impulses for adaptive ends; and for certain, as yet unknown, portions of nerve tissue, that of being permanently modified by each adequate stimulus, so that the reactions to successive stimuli of the same kind vary in intensity.

The reactions of a given animal or species are governed by the nervous mechanisms it has evolved, — by the forces to which its nervous system has been attuned. In other words, the complex organism differs from the simple only in the number of its reacting units and their attunement. It would seem, therefore, that the manifold reactions of man differ only in number and complexity, but not in principle, from the simple adaptive reactions of Venus' fly-trap in catching and digesting its insect food.

The Typical Adaptive Reaction

Venus' fly-trap, which is found in the damp, infertile regions of North Carolina, possesses one of the most remarkable adaptive mechanisms in nature. Darwin has given a graphic description of this plant in his volume on "Insectivorous Plants." Its body is composed of two plump leaf lobes, set nearly at right angles to each other, like the pages of a book held partly open, each lobe being fringed on the outer edge by a single row of sharp thorn spikes, which interlock like the gates of a prison behind the unfortunate insect

which chances to alight upon the surface of the leaf, or even to brush lightly against one of three tiny, hair-like filaments which project upright from the surface of each lobe, are about one twentieth of an inch in length, and form the receptor mechanism by which the plant is warned of the presence of its live prey. (Fig. 5.)

The moment a small insect touches one of these exquisitely sensitive filaments, the two lobes come together quickly, the marginal spikes interlocking, first at their tips, then down their entire lengths, while the edges curve inward to form a shallow miniature stomach, which begins at once to secrete digestive fluid if the object caught contains animal matter. If that object proves to be not of animal nature, but a bit of wood, of cord, of paper, or of other non-nitrogenous substance, the lobes will reopen within twenty-four hours, and it may be seen that no digestive fluid has been secreted. On the other hand, if a piece of gelatine, of cooked or raw meat or of albumin be substituted for the live insect, provided it weighs about the same as the usual insect prey, the lobes will close quickly, the digestive glands will become active and the process of digestion and assimilation will proceed in the normal manner. In this case, as when real insects are caught, the leaves remain closed for many days. If the filaments be struck forcibly by a needle or other hard object, no reaction will take place. On the other hand, if the filaments be touched lightly, so that the touch of an insect's foot is fairly well imitated, the lobes will close. Any touch either lighter or heavier than that of an insect invariably fails to elicit a response.

Drawing by Wm. J. Brownlow.

FIG. 5. — VENUS' FLY-TRAP (*Dionæa muscipula*) (Linnæus).

A. Plant and blossom.
B. Detail, lateral view of expanded leaf.

Venus' fly-trap thus evinces just as much power of perception and discrimination as is shown by the amœba; indeed, almost as much as is exhibited by many highly differentiated organisms, such as the frog, for example. The fly-trap catches flies, eats and digests them and ejects the refuse. The frog does the same, responding to the adequate stimulus of the sight of a fly as the fly-trap responds to its touch. Both the frog and the fly-trap catch insects by comparable motor mechanisms. Each depends on an adequate stimulus for the excitation of the mechanism as a result of which stored energy is set free to be manifested in the fly-catching reflex. Each then digests and assimilates the caught insect and when hungry catches another insect.

If the reactions of the human organism be reduced to their simplest terms, probably none will be found more intricate than this food-catching reaction of Venus' fly-trap and the frog. The principal difference between these three living mechanisms is rather a difference in the range of activation by environment, resulting in the frog and in man in a larger number of reactions which in turn involve more complex effector mechanisms than are possessed by the fly-trap. Each reaction of man doubtless has more component parts than each reaction of Venus' fly-trap, just as a large house contains more bricks than a small house. The most complex machine ever invented by man looks like a grotesque monster to the savage; yet its complex movements are compounded of the two simple movements of translation and rotation.

Three Stages of the Typical Reaction

Analysis of the reaction of Venus' fly-trap shows that there are three distinct stages in the process: the *adequate stimulus,* supplied from without by the insect touch; the process of *conduction* of the stimulus from the tip of the filament to the effector motor mechanism of the plant, performed in this case by a chain of tissue cells which in a certain sense resembles the specialized nerve paths of man; and finally, the *chemical and motor end effect,* involving all the acts and organs used in the closing of the lobes and the killing and digestion of the insect.

We have seen that the presence of the insect stimulus is necessary to excite the closing of the lobes, and furthermore, that it must be a specific or *adequate stimulus.* A touch, lighter or heavier than that of the insect, does not stimulate. Only the stimulus which throughout evolution has led to the development of the responsive mechanism in the plant can now activate that mechanism. Conversely, as soon as the appropriate force is applied, the characteristic reaction takes place, and will go on taking place as long as there is sufficient energy available in the plant. These observations agree with those recorded by Bose in "Response in the Living and Non-Living," and "Comparative Electro-Physiology." Bose shows that a wide variety of plants exhibit, under stimulation, phenomena which are identical with those generally supposed to be characteristic of animal tissues only; namely, fatigue under often repeated stimulation; the tendency to exaltation of the response during the early

repetitions of the stimulation; the lowering of response by depressants; and the abolition of response by poisons. In our own laboratory we have by experiment shown that the energy of Venus' fly-trap, like that of man, can be exhausted by repeated stimulation; that, as in man, its energy may be restored by rest; and that it may be anesthetized by the agents used in anesthetizing man.

In the three separate stages of *adequate stimulus, conduction* and *end effect* which compose the reaction of Venus' fly-trap, we find all the essential factors which enter into the life activities of man. Under *adequate stimulus,* for instance, are included the activating stimuli produced by heat and cold, dust, débris, microörganisms, food, air, water, light, poisons, blows, — by certain physical and chemical changes within and without the body, to which man through evolution has become "adapted" through the creation of an adaptive response. *Conduction* is supplied by the central and autonomic nervous systems, that is, by the organs of touch, taste, sight, smell, hearing, pain and by the chemical receptors for the initiation of certain reactions of chemical control. *End effects* are found in all the vital processes of motion and emotion, muscular activity, chemical change, psychic states, growth, nutrition, reproduction, thought, invention, social forms, government, war, religion, business, — in short, in all the activities by which man's life is distinguished from the immobility of the rock. In other words, magnification of the typical motor and chemical response of the sensitive plant gives us a concrete illustration of the premise stated above, that

all life processes result from the immersion of a sensitive structure in an activating environment. *Adequate stimulus* represents the environment; *conduction* represents the mechanism of communication; and *end effect* represents life itself in all its manifold expression.

The production of a simple adaptive motor act in response to an external physical stimulus is a *reflex*. The combined processes represented by *adequate stimulus, conduction* and *end effect* are known as reflex arcs. There are many such reflex arcs in the organism, which can be easily differentiated into their component parts — *reception, conduction* and *end effect*. Such reflexes are the contraction of the iris in response to light, and the winking of the eyelid in response to excitation of the conjunctiva. There are other reflex arcs, however, which, according to our conception, are built on the same plan, but whose component parts it is far from easy to determine. It is not easy, for instance, to define the specific, visible physical agents in the external environment which are responsible for the reflex actions manifested by a benevolent deed, by an artistic production, or by an intellectual process, even though we know, in a general way, that by natural selection the structures which manifest these responses have been developed as those best fitted to survive. Equally difficult is it to identify the forces which are responsible for the development of the intricate and obscure processes of metabolism, of respiration, of heart beat, of immunity or of reproduction.

Action Patterns

Somewhere in the tissues of Venus' fly-trap and of other organisms having reflex arcs there exists a tendency always to produce the same response to a given stimulus, that response being achieved by means of a mechanism acquired for its performance by natural selection. This mechanism may be described as a *scheme* or *pattern of action*, a pattern specific to that organism and possible of excitation only by *that stimulus which gave rise through selection to the mechanism itself.* Upon the number of his "action patterns" and the responses which are elicited by their excitation depend the life processes of the individual organism — whether man or lower animal. The exact nature of the *motor* or *action pattern* we are not prepared to discuss. For the present it is sufficient to state our belief that every adaptive reaction corresponds to the plan of the muscular reflex — occurring automatically in response to a primary excitation from without and being accompanied by a discharge of potential energy which may be measured by the depleted vitality of the organism. We consider also that every adaptive reaction is expressed in heat or motion in whatever form is of use to the individual.

As we have seen, the presence of the adequate stimulus is the first requisite for reaction. As the lobes of the fly-catching plant close only upon the arrival of the insect stimulus, so every conceivable act, thought or function of the human body requires an adequate stimulus for its manifestation, that manifestation depending absolutely upon the previous experience of

the organism or of its species with that stimulus. That is, the response to any stimulus depends wholly upon the biologic necessity which led to its evolution. The response to a sharp blow by pain and retreat from the offending point; the response to an insect-like tickle by the desire to scratch; the response to a soft caressing contact by pleasure and approach, are all specific to the species and the self-protective necessities as a result of which they were evolved in the organism. Similarly, the more obscure and delicate responses of thought and sentiment, of "study," "invention," "ambition," "industry," "joy," "sadness," "remorse," are all dependent upon specific stimuli in the environment and are specific to one or another of the biologic purposes of self-preservation, nutrition or procreation. That is, according to its phylogeny and its ontogeny, the life of any being may be completely defined in its *action patterns*. Conversely, given its *action patterns*, we should be able to predict the future action of any individual in response to any stimulus.

Action patterns, as may be seen, are synonymous with "associative memory," with "mind," with "intelligence," with "individuality." The single action pattern of Venus' fly-trap makes up its limited life and constitutes all it has of "mind." The larger number of action patterns in the more worldly experienced frog constitute its life and its correspondingly limited "mind." The multitudinous *action patterns* of man, representing every phase and degree of animal existence, constitute man's life and man's "mind." Life epitomized thus as the result of a structure played upon by the environment may well be compared, as

poets have often compared it, to a splendid symphony composed of notes to which the strings of the human instrument have become attuned and to which they respond when stimulated by the surrounding environmental forces.

The Principle of the Final Common Path

According to Sherrington the organism of man is integrated to respond as a whole to any adequate stimulus, this integration being accomplished mainly by the nervous system through the medium of the brain. The brain responds to but one stimulus at a time, although it acts with such rapidity and with such capacity for kaleidoscopic changes that it seems to be performing a number of acts simultaneously. That stimulus which secures possession of the brain over all other stimuli which are simultaneously striving for entrance is said to possess the *final common path* — an expression introduced by Sherrington. *The final common path is always the path of action.* Could every ceptor of the body be stimulated simultaneously, the brain, hence the body, would respond to but one stimulus, that being the one which has proven most important to the survival of the race. Could every ceptor of the body be *equally* and simultaneously stimulated, — that is, with the same (phylogenetic) force, — there would be no action. Could the pain ceptors of an animal be equally and simultaneously stimulated, there would be no pain. The attempt of the brain to discharge energy in response to one stimulus would be balanced by the other stimuli and inaction would result, or even death might occur. If the body were immersed in

great heat, for example, the body proteins would coagulate, but death would be painless.

In taking possession of the final common path, stimuli observe a definite order of succession. The stimulus which secures possession of the final common path at any moment is always the stimulus which phylogenetically is the most important. For example, stimuli threatening death or fatal injury will take precedence over stimuli presaging slight physical discomfort or the acquirement of food. Thus, in the simultaneous arrival of a flea bite and a heavy blow a man would be unconscious of the bite and would feel only the blow. Moreover, a physically or phylogenetically less intense stimulus already in possession of the final common path can at any time be dispossessed by a stronger stimulus or one of more phylogenetic importance. Thus, an animal in enjoyment of its food, or a hunter in search of small and harmless game, would each drop his occupation and flee in terror at the sudden apparition of a powerful advancing enemy. Thus, the schoolboy may have his desire for learning dispossessed by a pin prick administered by a neighbor; but if the schoolhouse were to catch on fire, the pin prick would be unnoticed and primitive fear would assume control of his motor mechanism.

The Threshold

The order of precedence of stimuli is, to a large extent, determined by what is known as the *threshold*, or the amount of resistance which each stimulus has to overcome before it excites action. Each incoming impulse, somewhere in its path to the brain cell, or

just beyond, encounters this resistance to its passage, which varies in degree for every impulse, as well as for the same impulse from day to day, from year to year, from experience to experience. When resistance to the incoming impulse is great, the threshold is said to be "high"; when it is small, the threshold is said to be "low." Repeated response to any stimulus lowers the threshold to that stimulus. The conditions which govern the threshold are of material importance to the individual. On the state of his thresholds to various stimuli depend a man's capacity for education, his habits and conduct.

The threshold is responsible for the fact that no more than the required energy is discharged in the consummation of a given act, as it is also for the condition which makes it possible for an individual to profit as well as to suffer by past experience.

Summation

The result of any given stimulus depends upon both the height of the threshold and the intensity of the stimulus. Response may also be hastened and intensified by repeating the stimuli at sufficiently short intervals of time to produce a cumulative effect. This is *summation*. In the conversion of energy for adaptive purposes the principle of summation plays an important rôle. If drops of water are allowed to fall upon the skin at such a rate that the effect of the stimulus of one drop has not passed before another drop falls in precisely the same spot, there will be a gradually increasing sensation in that spot, rising finally to an unbearable degree of pain. The threshold to

the stimulus is progressively lowered by each succeeding application, and the facility of energy discharge is correspondingly increased until a period of maximum discharge is reached. Another example of summation is the increasing sensitiveness to pain felt by a patient, who for a long time has had to submit to frequent painful wound dressings.

In a larger sense, the behavior of the individual illustrates summation. The facility with which energy is discharged in response to any stimulus is the result of the evolution of the responding mechanism through natural selection (phylogeny); and of the individual's own past life (ontogeny). Moral as well as physical efficiency may justly be regarded as the result of summation. In the training of athletes, where superior strength of certain sets of muscles is desired, efficiency is the result of the repetition of exercises which involve muscular action — activation of certain action patterns — at such intervals that the upbuilding effect of one action is not lost before a new exercise is given. Thus a gradual ascent to the maximum efficiency is realized. The principle of summation plays a similar important rôle in the production of certain pathologic phenomena, a progressively lowered threshold being largely responsible, for example, for such conditions as neurasthenia and mania.

An understanding of the mode of action of *adequate stimulus*, *final common path*, *threshold* and *summation*, upon which are constructed the action patterns which constitute man's motor adaptation to environment, assists in making more clear much that seems complex and confusing in human action.

Individuality and Action Patterns

Up to a certain point the activating environment of most motor beings is the same, and to that extent their structure, their "life," their *action patterns* (response to identical stimuli), are the same. Animals, for instance, breathe the same air, eat approximately the same food, suffer from the same microörganic invasions, are influenced by the same elements of climate. It is not surprising, therefore, to find them exhibiting the same general details of structure for respiration, circulation, digestion, reproduction; the same organs of secretion and elimination; of taste, smell, sight and hearing; the same quality of epithelial covering for internal organs; and the same chemical reactions in response to foreign proteins and inorganic substances in the body. These common structures, responding identically to identical stimuli, represent the extent to which self-preservation and species preservation depend upon the same elements. Variations in structure correspond to variations in the activating environment, the most important structural changes being the result of the requirements for survival in the conflict with other organisms.

In like manner it is as a result of the environmental stimuli in human relations that the *action patterns* of man have come to differ from those of other more closely allied animals, that difference being most plainly marked in a more highly evolved brain and central nervous system, in which are held the patterns for vast numbers of complex self-preservative actions unknown to other animals.

The action patterns of each species definitely represent the processes employed by that species for self-perpetuation — that is, for adequate defense against enemies, for securing food and for procreation. The action patterns of a turtle, a cobra, a sparrow, a fish or a man are specific for each of those animals, and would be useless if transferred from one to another species. The action patterns of a lion would not do for a deer, nor the patterns of a hawk for a chicken, and were the crossing of such phylogenetically alien species possible, confusion would be the fate of the unfortunate offspring, endowed with the action patterns of each parent. In the case of the offspring of a deer and a lion, for example, the hybrid would be compelled to experience toward every animal a simultaneous desire to attack and to flee.

The same external agency in an environment common to several organisms may excite vastly different action patterns in the different brains which it stimulates. Thus, if the image of a hawk were to fall simultaneously upon the retinas of a chicken, a cow and a boy, there would be created three separate action patterns specific to the phylogenetic experiences of these different individuals. The chicken, because chickens have ever been preyed upon by hawks, and only those which flew and flew quickly at the approach of one have survived, will be activated to flight, not because of any power to "reason" about it, but because natural selection has eliminated all chickens which have not automatically fled at the sight of a hawk. The cow, on the contrary, since hawks have exerted no selective influence on it or its species

through the ages, will be neutral and unmoved; while the boy, according to his phylogenetic and ontogenetic experience, either will idly watch the hawk or will try to shoot it.

Within the species, the experience of the family and of the clan takes the place of the experience of the race in evolving through selection more obvious minor structural and functional differences of manner and habit, color, facial expression, bearing, etc., which distinguish one group from another. The experience of the individual, in turn, will accentuate, neutralize or eliminate given family tendencies and establish new thresholds and action patterns, according to the old, the absent or the new stimuli encountered in his environment.

The extent to which the principle of action patterns and of the automatic specific interaction of stimulus and response helps in the interpretation of physiological processes will appear as our material develops and some of the more obvious specific responses are demonstrated.

CHAPTER III

ADAPTATION BY MEANS OF CONTACT CEPTORS

The Receptor Organs

In the foregoing chapter we stated our viewpoint that the nervous system of man, like other organic structures, is the product of the selective adaptation of the organism to its environment; and that the nervous system acts as a conducting mechanism for the specific energies or stimuli of the environment which evoke the adaptive reactions of the organism. For the reception and transmission of environmental stimuli receptor organs have been evolved. A study of the distribution and relative activities of these mechanisms epitomizes the story of the adaptation of the whole organism. In that of man and of all other multicellular organisms there are presented to the environment two fields of contact in which receptor organs are implanted: an outer surface of skin and mucous membranes, which are exposed to every vicissitude of climate and contact, and inner organs and connective tissue, which are partially screened from the outer environment, but are subject to a variety of physical and chemical changes within the organism itself, these changes, however, being primarily induced by the larger reactions initiated by the ceptors of the outer surface. Imbedded in the cellular

masses of both the inner and the outer body surfaces are numerous nerve endings, adapted to the reception of specific stimuli.

These specialized nerve endings are classified as *contact*, *distance* and *chemical ceptors,* according to their distribution and the means by which each elicits its own specific response in the organism. *Contact ceptors* are distributed throughout the surface layers of skin and mucous membranes and apprehend all *bene* and *noci* impulses contributed by direct physical impacts, such as the impacts of stones, dust, débris, external heat and cold, wind and water, food, stings of insects, mechanical injuries and irritations of all sorts. Included among the contact ceptors are the touch ceptors; the specific ceptors which initiate sneezing, coughing, winking, swallowing, vomiting, hiccoughing, peristalsis, evacuation of the urinary bladder, of the gall bladder and ducts, of the uterus and tubes, of the kidney, of the rectum; and those ceptors which are concerned in many other protective reflexes throughout the body. Stimulation of the contact ceptors results in a quick discharge of energy for local motor acts, and are of special use in guiding the animal away from injurious contacts that threaten his well-being, and toward beneficial contacts that result in nutrition and procreation. Were the animal deprived of his contact ceptors, his vital processes might be carried on by means of his *distance* and *chemical ceptors*, but paralysis of the motor acts of ingestion and elimination would soon result in death by starvation, or by poisoning from deleterious unejected waste matter.

The *distance ceptors* are concerned principally with

the apprehension of objects in the distant environment and the orientation of the animal *as a whole* toward or away from them, in accordance with their significance in the life of the individual or the species. Such are the ceptors for sight, hearing and smell, by which the animal perceives its enemies, its prey or its mates, and by which it is enabled to conduct itself in relation to an environment otherwise unknown to it. Distance ceptors involve the action of the whole organism rather than its local parts, as is the case with contact ceptors, and *expedite* the motor acts which are ultimately consummated by means of impulses received through the contact ceptors. Thus the sight and the smell of food lead to its acquisition, and incidentally to a more speedy acquisition than would follow were the animal deprived of distance ceptors and forced to blunder blindly about on the chance of coming in contact with food. The advantage to the organism of thus being able to react to objects at a distance goes far toward achieving the survival of the species.

Like the contact ceptors, the distance ceptors, on adequate stimulation, give rise to a discharge of energy for an adaptive reaction. Stimulation of the contact ceptors, however, leads to short, quick discharges of energy for local motor acts which involve a comparatively small part of the organism, while stimulation of distance ceptors usually inaugurates a continuous expenditure of energy for a long series of physical and chemical reactions involving the organism as a whole and consuming large stores of energy. For example, stimulation of the contact ceptors of the hand of a child who plays with fire will cause a momentary discharge of energy

with a consequent quick retraction of the hand and arm; while in the same child stimulation of the distance ceptors of sight by the image of a pot of jam on the pantry shelf will cause a continuous discharge of energy for a long series of motor acts.

Had distance ceptors never been developed, life would have remained on the plane of stationary animals, such as the sponge. The inner processes, those connected with circulation, respiration, digestion and elimination, might have been developed through contact stimulation, but incentive to penetrate into the distant environment would never have been realized. In other words, the evolution of distance ceptors in animals is correlated with the evolution of their powers of free movement.

In his work on the "Integrative Action of the Nervous System," Sherrington clearly emphasizes the important connection between distance ceptors, locomotion and the upbuilding of the higher brain functions, and gives some interesting confirmatory examples of the simultaneous disappearance of sense organs and loss of locomotion in animals which metamorphose from an active motor life to one of a sedentary character. Certain species of the *Ascidia* and barnacles, for instance, are animals which are suddenly transformed from a larval life of active locomotion to one of inactivity when in the course of their development they become attached to some fixed object in their environment. The *Brachiopod*, for example, at first possesses a locomotor mechanism and a well-developed visual organ. When it suddenly relinquishes larval life and becomes permanently attached to a fixed object, the highly de-

veloped eye degenerates and disappears. A similar transformation occurs in the free-swimming *Ascidian*, which likewise begins life with a comparatively highly differentiated nervous system, consisting of a brain, a spinal cord and a well-developed eye. Like the *Brachiopod*, it becomes attached to a stationary object and the highly developed nervous system, of use in its motor life, disappears.

The *chemical ceptors* for the apprehension of stimuli and the initiation of purely chemical reactions are distributed throughout the inner tissues. Chemical ceptors are found in the linings of the stomach and intestine, in the brain and in the medulla. They govern respiration and circulation; they govern hunger and thirst; and, by maintaining the standard of chemical purity of the body, they govern energy transformation. Upon adequate stimulation the chemical ceptors give rise to reactions which are in all respects as specific and adaptive as those initiated by the contact and distance ceptors. Although they are among the most obscure and elusive of adaptive mechanisms, the chemical ceptors present some of the most striking examples of specific reflex action in the organism.

Contact Ceptor Mechanisms

In the functions of contact, distance and chemical ceptors is to be found a remarkable confirmation of the law of specific response, a typical illustration of which is the adaptive reaction of Venus' fly-trap.

Wherever in the organism mechanisms for the reception of contact stimuli exist, they are in type and function specific to the biologic needs of the area in which

they are implanted. The adequate stimulus for each one of these mechanisms is some agent in the environment which originally occasioned the development of that mechanism in the organism. The response to the stimulus is invariably some act by which the organism is protected or the welfare of the species promoted.

The response to a stimulation of the ceptors of the skin by heat or mechanical injury is a type of pain which is specific to the form of injury. Stimulation of the contact ceptors of the membranous lining of the nose produces a sneeze, leading to the expulsion of the harmful obstruction. Stimulation of the membrane of the throat, pharynx or larynx produces a cough, whose purpose is the expulsion of the source of irritation. Stimulation of the esophagus produces a swallowing movement; of the lining of the stomach and of the muscular wall of the intestine, peristalsis; of the interior walls of the uterus and tubes, of the gall bladder and ducts, of the urinary bladder, of the ureter, of the kidney or of the rectum, contractions which are specific to those regions, resulting in the expulsion of their contents. In no case could any of these mechanisms, each adequate to the protection of its particular field, be interchanged with another to initiate an act of protection. Stimulation of the cornea of the eye cannot produce a sneeze; irritation of the nose cannot produce a cough; contact with the skin cannot produce peristalsis.

In no case is any mechanism superfluous. Although some mechanisms, such as the scratch reflex, may show evidence of a vast antiquity and a dwindling usefulness, the organism as a whole is far from being sufficiently

equipped with protective reflexes whereby to withstand all the harmful mechanical agencies that menace its survival. The lack of protective response to the X-ray, for instance, is but one of many similar instances of the lack of protective mechanisms against lately evolved menaces to human life.

In the areas and organs which through the ages have been most exposed to direct contact with environment, we find the greatest number and the most complete systems of adaptation to the common harmful and beneficial agencies which are encountered in the environment. Thus, in the skin and exposed mucous membranes we find the most plentiful distribution of ceptors in those regions most open to environmental contacts. In the mechanism for the protection of the eye and the nose we have a symbolic suggestion of perennial flying dust and débris, which always must have imperiled the organism by assailing those important organs. In the abundant ceptors for touch on the hand and for taste on the tongue, we have proof that it was always at these points that objects to be apprehended or swallowed were first encountered. The location of the ceptor mechanisms tells a vivid story of the development of the organism, of the chief dangers which have threatened and the chief benefits which have exerted a positive influence upon the survival of the species. On the other hand, the absence of ceptors gives equally suggestive testimony regarding the phylogeny of the species. On the basis of the presence and the absence of ceptor mechanisms, therefore, we may infer and reconstruct much of the past history of the organism.

The Tickle Reflex

Of similar significance is the not infrequent appearance of a mechanism of little or no present value to the organism; for just as the organism is slow in evolving adaptations to newly developed factors in the environment, it is slow in discarding adaptations to an older environment, even such as may be a hindrance to life under present conditions. Such a relic of prehistoric perils is the tickle reflex. It is more strange than appears at first glance that the tickle reflex can be excited only in certain parts of the body, by but two types of tactile impression, and that it is invariably accompanied by a self-protective reaction. One type of the tickle reflex is elicited by a light running motion on the surface of the skin, which produces a sensation like that produced by a crawling insect, with an irresistible desire to scratch or rub the affected part. A sharp impact causes pain, but if the adequate stimulus of contact which simulates the crawling of an insect be applied again and again in the same spot it will cause each time the same tickling sensation. This reflex was undoubtedly developed at a time when insects were a great menace to life, and when only those individuals which evolved an effective defense were able to prevail. It may even supply an explanation of man's loss of hair in the upward march, since the presence of hair would provide ambush for the insect enemy, and its loss, together with the evolution of the tickle sensation, would greatly facilitate defense.

Although the need of this gross adaptation against the attacks of insects is steadily waning as more subtle

methods of adaptation advance, — sanitation, drugs, clothing, etc., — yet insects still menace man's welfare, even his life; the mosquito is still the most active agent by which malarial fever and yellow fever are disseminated; by the bite of the flea, man may be inoculated with bubonic plague; and sleeping sickness may result from the sting of the tsetse fly.

A second type of tickle reflex is elicited by heavy penetrating pressure in the region of the ribs, the loins, the base of the neck and the soles of the feet — the pressure simulating the penetrating contact of a tooth-shaped body. The reaction in this case is a violent discharge of energy in the form of laughter with cries for mercy and frantic muscular efforts to be free if the stimulus be continued. If one were tied hand and foot and were vigorously tickled for an hour, he would probably be as completely exhausted as if he had run a Marathon race or sustained a crushing injury; indeed, victims of torture in the Middle Ages were often killed by prolonged tickling.

The fact that these ticklish areas are found in those parts of the body which are still and must always have been the points most frequently attacked by savage beasts leaves little doubt that this reaction developed at a time when man's progenitors, like the carnivora to-day, fought their enemies face to face with tooth and claw, and that this mechanism was acquired as a means of protection against valiant foes. (Fig. 6.)

There is abundant evidence to bear out this conclusion. Children and young animals at play invariably recapitulate the fight maneuvers of their ancestors by attacks in ticklish spots. Playful puppies in frolic

Drawn by W. J. Brownlow from Dr. A. E. Brehm's "Life of Animals."

FIG. 6. — CONTEST BETWEEN ANT-BEAR AND PUMA.

This attack with teeth and claws upon unprotected parts illustrates the method by which deep ticklish points may have been evolved, and explains why trauma of these parts produces the greatest shock.

bite each other in their ticklish points, giving a mimic representation of ancestral fights, as well as of fights to come. Children commonly and with glee fling themselves upon one another in the same attitude; one

youngster, the weaker, flat on his back, with arms and legs upraised, fights playfully in self-defense, while the other, on top, pummels and claws him in neck and ribs in a playful effort to excite him, the mimic contest not infrequently terminating in a real fight in which the same parts are vigorously attacked.

The fact that animals fight effectively in the dark and always according to the habits of their species would seem to suggest strongly that fighting is not an intelligent occupation, but a reflex process, dependent solely upon the infliction of blows in responsive areas; and to be explained, as Sherrington explains the reflex processes of walking or running, as a succession of varying pressures occurring in the feet, joints and limbs, by which is produced a series of stimulations and responses which appear in aggregate as the harmonious "habit" of locomotion.

The relation of tickling to laughter is an interesting feature of this reflex and will be referred to later when we discuss the phenomenon of laughter. Just now it is sufficient to note that there is no laughter in response to tickling by an insect, but boisterous laughter on stimulation of the deep ticklish areas. The expenditure of energy in each case is proportional to the phylogenetic demand of the original condition which gave rise to the reflex. Indeed each type of the tickle reflex is an excellent example of a specific response to specific excitation.

Phylogenetic Origin of Specific Reflexes

As the tickle reflexes have been developed in response to attacks by insects and carnivora, so other material

dangers, such as flying dust and débris, poisons, falling bodies, heat and cold, have added the reflexes of winking, coughing, sneezing, vomiting, fainting, shivering and sweating, which in like manner exemplify the adaptation of the organism as a whole or in part to specific menaces in the environment. Of all the ceptor mechanisms for protection the most wonderfully adequate are the mechanisms which guard the eye. In the primeval struggle, the injury or loss of this member, so vitally connected with all processes of nutrition and protection, meant instant death. And there were always myriads of agencies capable of accomplishing the destruction of the eye. There were the menaces of flying twigs and branches in the forest, of storm-driven dust on the plains, of the dry pollen of ripening plants, of the sharp edges of dead blossoms and leaves, of thorns and of stones. As a protection against these manifold hazards, there has been evolved a remarkable mechanism: a smooth, round, elastic little ball, incased in a transparent, glassy membrane, exquisitely sensitive to touch. This ball is protected by the lid which fits around the curve of the cornea and is rendered doubly effective by its hard, smooth margin and fine fringe of delicate lashes. This beautifully adapted lid closes instantly when a foreign body touches the cornea and its moist inside surface sweeps again and again across the surface of the cornea in an effort to dislodge the offending particle, while the lachrymal glands, being simultaneously stimulated, expedite the process of removal by pouring out a fluid which is admirably adapted to carry away the invader.

In like manner an especially delicate mechanism has

been evolved to protect the lungs from the invasion of foreign particles which might enter through the nose and throat. The perfect adaptation of this mechanism is manifested in the act of sneezing, which occurs when the lungs are threatened by a foreign body approaching through the nose. Breathing through the nose ceases instantly — that the foreign body may not be drawn farther inward; the mouth opens to take in a large amount of air, which is suddenly and violently expelled through the nose, effectively clearing the passage. The protective action is further facilitated by the simultaneous outpouring of mucus which, like tears, is excellently adapted to carry off deleterious bodies. The adaptive act of blowing through the nose is apparently a recent development.

To a foreign body in the larynx the adaptive response is a cough. The regular respiration is inhibited, but there is a cautious intake of air, followed by its violent expiration through the partially closed vocal cords, so that every portion of the upper mucous membrane is subjected to a thorough searching pressure. This reflex is of such value to the organism that it is ever active by night as by day, being wholly abolished neither by sleep nor by inhalation anesthesia.

Unlike the respiratory tract, the digestive tract is not efficiently protected against the entrance of harmful foreign bodies. The reflex responses to smell and taste are excellent guardians of this region, however, for they act as rigid censors of such deleterious matter as decayed food, putrid flesh and excreta. The universal repugnance of man and of some animals to the odor of their own excreta is evidence that this is an ancient and

important adaptation. That this is true of the act of vomiting also is shown by the extreme difficulty with which that reflex is dispossessed in the presence of other stimuli. Vomiting occurs in the midst of deepest emotion, of excruciating pain, during sleep and during anesthesia, even up to the very moment of death, in spite of the fact that it is attended by a widespread muscular activity, during which the glottis is closed, the diaphragm fixed, and the entire muscular apparatus of the respiratory tract thrown into the most violent contractions. Strangely enough, vomiting occurs almost exclusively among carnivora and omnivora, this fact suggesting an interesting comparison of the hazards of flesh with those of vegetable diet.

In the adaptations of many animals to cold and heat are to be seen some of the most characteristic responses to contact ceptor stimulation. Many animals are provided with structural protection against cold and heat by such variations in the body covering as fur, feathers, hair, wool, layers of fat and pigmentation. Among warm-blooded animals the most common reactions to cold and heat are shivering, sweating and the sensation of thirst.

An interesting adaptation of birds to cold weather is the phenomenon of "ruffled feathers," whereby in the spaces between the quills a warm envelope of air is retained around the body. Protection against cold by the prevention of heat radiation is secured also by the lowered respiratory rate which is common to most animals when they come into contact with cold. The habit of hibernation is an adaptation for protection against starvation rather than against cold, since for

those animals which hibernate prolonged cold means a period of lessened food supply.

The response to external heat by sweating and muscular relaxation is an effective method for reducing heat production and increasing heat elimination.

The Specific Response of Pain

In addition to these various protective mechanisms, there exists for the defense of the body the important phenomenon of pain. The pain which accompanies abnormal organic conditions will be considered in other parts of this volume, but the pain which forms part of the response to excessive light, to heat, to cold, to mechanical injury, to local anemia resulting from a cramped position, or to the pressure upon internal organs which presages the evacuation of their contents, is essentially a normal phenomenon and must be considered with other normal adaptations initiated by the stimulation of contact ceptors.

In type, location and intensity pain is always specific to the stimulus by which it is evoked. In addition pain is always associated with some form of muscular action by which the body moves away from, fights off, removes or expels from the body harmful agents or products or makes other muscular adjustments and adaptations. As we shall see later, pain is analogous in nature to the phenomena of the emotions which occur in response to distance ceptor stimulation and in an analogous manner expedite adaptive motor reactions.

A child puts his hand into the fire, and instantly recoils. A boy steps upon a sharp stone, and bounds away hastily. Pain is the precursor of each act. Pro-

longed pressure on any part of the body produces the pain of anemia which is followed by vigorous muscular activity to hasten the return of the normal circulation. Pain induces the emptying of an overextended urinary bladder, contractions of the large and of the small intestine to overcome obstruction, and delivery from the pregnant uterus. The most exquisite pain results from mechanical irritations of the cornea and is followed by a complicated muscular reaction. Pain of a specific type results from irritation of the pharynx, the larynx or the trachea, and in each case is followed by appropriate muscular reactions.

Like pain itself, the muscular activity which follows pain is specific in type, location and intensity to the exciting stimulus. That is, the muscular act of coughing, which follows the pain produced by an obstruction in the larynx, is specific to the menace in that area. The muscular act of scratching which accompanies the *quasi* pain of tickling is adequate for an insect's bite, but would be inadequate for the pain produced by intense heat or a heavy blow.

Pain Areas

In order to discover the relative distribution of contact ceptors in the body and to confirm their adaptive origin, we undertook an extensive research upon animals subjected to various types of trauma, *while under ether anesthesia.* We have stated already that the result of any stimulus is to cause a transformation of potential into kinetic energy for an adaptive reaction; this adaptive reaction in the case of mechanical injury being some form of muscular activity tending to protect

the injured part. In previous books and papers[1] it has been shown that unconsciousness produced by inhalation anesthesia does not interfere with *certain* discharges of energy in response to physical injury, and that, except for the absence of pain and muscular action, the ultimate effect of trauma under anesthesia is the same as if the injury were inflicted upon a conscious animal. In other words, with the exception of the diminished or absent response of the skeletal muscles, the reaction of an anesthetized animal to a certain degree of trauma is comparable to the reactions of a conscious animal to the same trauma. This reaction includes an increased respiratory and heart rate, a disturbance of the blood-pressure, an increased acidity of the blood and the urine and — if the injury inflicted be sufficiently great — histological changes in the brain, the liver and the adrenals.

Since in some degree all the physiological phenomena above enumerated attend upon every activation, any one of them may be taken as an index of the entire process. In our investigation of the effect of mechanical injury upon various parts of the body the blood-pressure and the respiratory rate were taken as an index. That is to say, if injury to the paw of a dog caused a rise in blood pressure and increased respiration, these changes were regarded as indices of the total stimulation, and as an evidence of the existence of pain ceptors in the part producing the response.[2] If on traumatizing a given region no change in blood-pressure or

[1] G. W. Crile: An Experimental and Clinical Research into Surgical Shock; G. W. Crile and W. E. Lower: Anoci Association.

[2] In the abdominal region a fall, not a rise, in blood pressure occurs. If trauma causes any change in the blood-pressure, whether it be a fall or a rise, the presence of contact ceptors is indicated.

respiration was noted, and no corresponding histologic changes were found in the brain, the adrenals or the liver, we assumed that these were pain-free areas, that is, that they contained no contact ceptors.

In our experiments we found, moreover, that the nature of the response to trauma under ether depended not only upon the location, but also upon the type of the injury. In other words, our investigations showed that the more a given part, by reason of its position, was exposed to injurious contact with environment during the vast periods of evolution, the more thickly is it sown with contact ceptors: and that the more nearly the artificial injuries resembled those probably encountered in the phylogenetic past, the more immediate and vehement was the response elicited. Thus, when the skin of any part of the body was burned, cut or torn, there was a prompt rise in blood-pressure, indicating the presence of the many contact ceptors which had been developed to protect the body against the many harmful contacts of like nature which must have assailed the naked body throughout phylogeny.

As would be expected, the skin of the extremities was found to be more keenly sensitive than that of any other part, for it has been ever by means of its extremities that the animal has first met the material obstacles in its path. It was by means of contact impressions that the organism first distinguished the good from the evil in its environment. Injuries to the paws of an anesthetized dog — cutting, crushing, fracturing, amputating and burning — were attended by a sharp rise in blood-pressure, followed by

a fall; and the respirations increased in frequency and became irregular. These responses are identical with those which follow the crushing or burning of the hand of a conscious human being.

Injuries to the muscles of the trunk and extremities caused a rise in blood-pressure similar to that caused by cutting the skin. The rise was more marked when the muscles most exposed to attack were injured — such as the muscles of the extremities and abdomen — and was less marked when the protected deep lumbar muscles were injured. When amputating the hip of a dog, the skin incision alone caused almost as much change in the circulation and respiration as was caused by severing the entire muscular mass of the thigh. The cutting, burning and tearing of connective tissues — fascia, tendons and ligaments — produced little or no appreciable effect on the blood-pressure.

Injury of the bone disclosed the fact that roughly cutting or separating the periosteum caused a slight rise in blood-pressure, while no alteration in blood-pressure or respiration was produced by sawing, curetting, cutting or crushing cartilage or bones from which the periosteum had previously been removed. In the fact that injury to the interior of either the large or the small joints is likewise attended by little or no response, we have seemingly a curious inconsistency. It might be explained on the ground that a crippled animal would have scant chance for life in the wilds. His superior foes would certainly overpower him speedily, so that there would be no opportunity for the development through survival of a protective mechanism.

In traumatizing the peripheral nerve trunks we found that the type of injury had an important bearing upon the response elicited. Thus the dragging, pulling, tearing and contusing of nerve trunks produced marked changes in the blood-pressure and respiration. Thermal irritation caused an even greater rise in blood-pressure; but if the nerves were severed quickly with a sharp knife, the resultant response was slight. There were no hostile animals or agencies in the phylogenetic environment whose instruments of attack approximated the exquisitely sharp scalpel of the surgeon.

Everywhere about the head and neck, as we have noted, there is an adequate provision of self-defensive mechanisms. Yet in a general traumatization of these parts it was noted that apart from the keen sensibility of the skin covering, there was no abundant distribution of contact ceptors. If the eyes, the conjunctiva, the eyeball or the optic nerve was injured, there was occasionally a slight though scarcely perceptible change in blood-pressure. The adaptive response here is confined chiefly to winking, which exerts but slight demand on the general muscular system, hence no circulatory changes are seen. But such injuries as the contusion, laceration or dilatation of the nostrils were met promptly by a distinct rise in the blood-pressure. In this case a vital function of the body — respiration — was threatened. The response was equivalent to that frantic fighting to be free which follows any attempt to obstruct the nostrils of any animal or of man. For the same reason, mechanical injury of the interior structures of the throat and mouth produces a change in blood-pressure, when injury to the respiratory function is threatened. The

inner structures of the mouth, where contact with environment is confined chiefly to the intake of food, have had scant opportunity to evolve any important defense mechanisms beyond those guarding against the ingestion of improper food.

The same loyalty to the respiratory function and indifference to other menaces was manifested by the larynx, trachea and esophagus, when these parts were subjected to injury under anesthesia. Instant arrest of the respiration was caused by even gentle contact with the mucous membrane of the larynx at any point from just below the vocal cords to the upper laryngeal opening and the under surfaces of the epiglottis. Injuring the trachea caused coughing, but injuring the esophagus caused no response. Extensive dissections of other tissues of the neck caused no disturbance of the blood-pressure and respiration provided that the vagi and sympathetic nerves were uninjured.

For the protection of the master organ, the brain, there has been evolved the most adequate of structural protections — namely, the skull. In accordance with the premise that contact ceptors have been developed only in those parts of the body that have been exposed to the environment, one would expect to find none within the brain, which has always been shielded by its bony covering. To test this point, the brains of anesthetized dogs were exposed and one hemisphere of each was subjected to trauma. No change in blood-pressure or respiration was noted in any instance; and microscopic examination of the uninjured hemispheres showed no histologic changes. So complete throughout phylogeny has been this protection of

the brain from injury that if the skull has been previously opened under anesthesia, the brain of a conscious patient may be explored with a probe for a tumor or other lesion without causing the slightest pain — indeed, the entire brain could be removed without the patient's knowledge.

After the extremities, the greatest shock-producing areas of the body were shown to be the chest and the abdomen. The deeper areas, the organs in the retroperitoneal region and the muscles of the spine showed slight or no response to injury. Although injury to the chest wall causes pain, the heart may be pierced by a needle without pain. The heart, like the brain, has had no phylogenetic opportunity to evolve pain ceptors, and like the brain has always been a vital organ, the penetration of which meant instant death to the individual. The lungs likewise are pain-silent to gun-shot wounds, stabs, contusions and punctures. In opening lung abscesses no pain is caused by the penetration of the lung tissue.

Within the abdomen we found similar contrasts in sensibility, and here, too, the type of trauma determined the degree of shock. Thus, in our experiments, pulling upon, dragging and roughly manipulating the stomach and the intestines caused an immediate fall in blood-pressure, but a swift, keen incision, even the crushing and burning of the inert organ, held gently and carefully, caused no response. In the clinic a loop of intestine has frequently been brought into a wound for a few days and opened with a thermo-cautery, without pain. Internal hemorrhoids may be painlessly destroyed by burning.

Rubbing, dragging, pulling upon or tearing the parietal peritoneum caused a lowered blood-pressure, but the same injury inflicted upon tissues behind the peritoneum caused no marked change in blood-pressure or respiration. In our researches the liver was crushed and cut, the cystic duct was dilated, the kidneys were cut, crushed and contused, the spleen was excised — all these operations being performed without any appreciable effect upon blood-pressure or respiration, except when, by chance, in the process, contact was made with the peritoneal covering. While gentle handling of the urinary bladder, the uterus and tubes caused little change, specific injury, such as cutting, compressing and overdistending the bladder, the contusion, incision and rough manipulation of the uterus and tubes caused a rise in blood-pressure, which was especially marked when the full bladder was compressed, or when the uterus was roughly manipulated. Experiments upon the deeper tissues in the retroperitoneal space revealed the fact that the back and spine are almost as devoid of contact ceptors as are the brain, lungs and heart. Injury of the deep fascia, of the muscles or bones of the back caused but little effect on blood-pressure.

Now what is the meaning of this unequal distribution of contact ceptors? Our experiments have proved that the greatest number of contact ceptors are implanted upon the front surfaces and the extremities; that on the back there are few contact ceptors, while they are almost or entirely lacking in protected areas. The explanation is indicated by the type of trauma

which elicits the most powerful response to harmful stimulation of the contact ceptors of the chest and the abdomen. These areas are the ones that respond to tickling by a recapitulation of the combats of our ancestral animal enemies. Undoubtedly, the specific distribution of contact ceptors in the areas which have been the points of attack throughout the ages is another relic of this era of brute contest. The scanty equipment of the back and deeper areas with contact ceptors is evidence that whatever fighting was done, was done face to face and to the death. The silence of the vital organs is the eloquent silence of defeat, bearing testimony to the fatalities of the struggle, as the sensitive spots bear testimony to the hazards and escapes.

It remains to harmonize certain exceptional occurrences. We noted experimentally that direct injury to the gall bladder and cystic duct caused no responsive rise in blood-pressure. Yet, we know clinically that the passing of gall stones causes great pain. Likewise the experimental cutting and crushing of the kidney was attended with no response indicative of the presence of contact ceptors; yet the pain caused by the passing of kidney stones is intense. In these instances we have examples of pain as an adaptive response to pressure from within, its purpose being to incite the protective muscular activities of evacuation and expulsion of harmful contents. The same is true of the pain produced in the urinary bladder by pressure, and in the uterus and tubes by a reproduction of the normal type of stimulus which induces the evacuation of their contents. These organs, like the brain, are shielded from external

injury, but contact ceptors have been evolved from within by the forces of pressure or obstruction.

This study of the distribution of the pain areas in the body enables us to draw valuable conclusions in regard to the evolution of functional processes in the organism by factors in the environment. To recapitulate: The response to physical trauma is determined by two things: (1) By the type of injury inflicted, — that is, whether or not it approximates the injury inflicted during phylogeny; (2) By the region traumatized, — that is, whether or not it was exposed to injury throughout phylogeny. We see that injuries from artificial, extra-natural agencies, such as keen-bladed knives, fast bullets, radium emanations and the X-ray cause little or no pain or other response, while injury by tearing with blunt instruments, simulating the commonest type of phylogenetic attack with teeth and claws, or by bruising and crushing environmental contact, causes a swift and powerful response and pain.

We see that areas which have been commonly protected from contact with environment by an impervious outer layer of bone or flesh, such as the brain and the heart, to which penetration would have meant instant death, have developed no protective pain mechanisms, while areas which have been continuously exposed to injurious forces, such as the surface and extremities, are plentifully supplied with contact ceptors. Thus, deep and protected areas and organs, such as the liver, spleen and kidneys, are, like the heart, lungs and brain, almost devoid of contact ceptors: the back and spine are but sparsely supplied, while the exposed surfaces

of the palms of the hands, the tips of the fingers, the soles of the feet, the surfaces of the chest and abdomen, which have ever borne the brunt of attack, are thickly sown with protective mechanisms. Thus contact ceptors are more thickly sown upon the outer surface of the body, as compared with the inner, the front as compared with the back, the extremities as compared with the trunk.

We see that the contact ceptors respond to stimulation by all agencies which have exerted a powerful influence for life or death upon the species in the past, while they do not respond to such equally fatal, but lately developed, artificial agents as electrical currents, rifle bullets, keen-bladed knives, radium emanations and the X-ray. Had these agencies been factors in the environment throughout phylogeny, those species incapable of evolving mechanisms of defense, either of structural or functional character, would long since have been eliminated, as have been those in which there was evolved no means of defense against sun and wind, against insects and microörganisms, against poisons and deleterious food. As the harmful effects of any environmental agent, without awakening any neuro-muscular response, may injure or destroy other parts of the body than those exposed to their impingement throughout phylogeny, so these newly developed agents can injure the whole body without pain. A device of exquisitely sharp knives driven at a superlatively high speed might cut the body to pieces without exciting any neuro-muscular response.

In the absence, as in the presence, of these adaptive mechanisms, therefore, we are offered a rich glossary for

the interpretation of man's phylogeny. As the geologists have reconstructed the earth's past history from the evidence of fossilized remnants buried deep in its crust, so we may reconstruct the history of man's physical contact with nature from its effects upon his structure and its functions. As philologists found a key to the unknown, long-buried hieroglyphic language of ancient Egypt in the Rosetta Stone, so we find in the distribution of contact ceptors a key to that mysterious language of communication between the structure and the environment, which, being translated, tells of a racial experience that coincides closely with the incidents of geologic evolution, as we know them. That is, man has been evolved, much as other animals have been evolved, by fighting, by pursuing and being pursued, by crouching, grasping and killing, by cowering from the hostile wind and weather as he cowered from living enemies; by seeking out the warmth, moisture and sunshine, as do all living things to-day.

Law of Phylogenetic Association

But more than the past history of the species is revealed by this relation between mechanisms in the body and agencies in the environment. In our experiments we found that whenever we reproduced approximately one of the environmental stimuli which had given rise to adaptive responses in the organism, we evoked simultaneously a transformation of energy commensurate with the energy required for the phylogenetic response to that environmental stimulus. When we reproduced the insect stimulus by tickling,

there resulted a transformation of energy and a movement exactly appropriate to the phylogenetic association of organism and insect. In the recognition of this inevitable interaction is discovered an important biologic law — a law as absolute as is the law of gravity. It is the law of *Phylogenetic Association,* according to which the transformation of energy for adaptive ends is based upon the adaptive responses of the organism during its evolution. It is easy to show that responses to contact ceptor stimuli are in accordance with this law, for these reactions are readily divisible into their component parts. The responses initiated by distance ceptors are not so easily comprehended, however, as they are composed of a group or series of motor, chemical and sensory reactions which must be identified before their conformity to the law of phylogenetic association is established. Before discussing the reactions to distance ceptor stimuli, therefore, it is necessary to study the mode of action of the chemical ceptor stimuli.

CHAPTER IV

ADAPTATION BY MEANS OF CHEMICAL CEPTORS AND CHEMICAL ACTIVITY

THE division of the receptor mechanisms of the body into *contact*, *chemical* and *distance ceptors* indicates the adaptive power of the organism as evinced (1) by local cellular masses; (2) by the individual cells as separate entities; (3) by the organism as a whole. For, as we have seen, the response to heat pain by the removal of the injured part from the injuring contact is essentially the response of a part of the organism for the good of the whole. In like manner, such protective reactions as the response to excitation of the chemical ceptors in the stomach by food; in the respiratory centers by acidity; in the cortex by foreign proteins; in the mouth and nose by food and food particles, are responses of specialized tissue for the good of the whole animal, these reactions differing in kind but not in principle from reactions to excitation of the contact ceptors. Later, we shall see that the response to excitation of the distance ceptors is the response of the *integrated animal* for the good of the species.

The existence of chemical mechanisms of adaptation indicates the existence of an inner activating medium which is distinct from the outer activating environment. As the contact ceptors represent the factors

of an ever-changing world without the organism, so the chemical ceptors, implanted deep within the tissues, as well as to some extent on the surface, represent not only certain factors of that outer *entourage*, but more particularly the events of a ceaselessly active, ever-changing world within the organism.

As we shall later attempt to show, the phenomenon of metabolism may in a sense be regarded as an example of adaptation through chemical ceptors. The sensation of hunger which impels man to eat has its origin in chemical changes and is manifested by muscular contractions in the stomach, which in turn are induced by the condition of lowered nutrition in the body. The presence of food in the mouth is the adequate stimulus for the secretion of saliva, which, passing with the food to the stomach, becomes there the adequate stimulus for the outpouring of gastric juice. The impingement of this acid mixture upon the pyloric end of the stomach is the adequate stimulus for the rhythmic opening and closing of this gate, through which the partially digested mass passes into the duodenum and in turn becomes the stimulus which excites to activity the pancreas and biliary apparatus. In the intestine other glands are excited to action through the excitation of chemical ceptors and at last, largely through a series of chemical ceptor stimulations, the whole intake of food, unassimilable in the beginning, is prepared for absorption and use in the organism.

By far the most interesting examples of the adaptation of the organism through chemical ceptors, however, are offered in its mode of defense against foreign

proteins, infection, auto-intoxication and the toxins of pregnancy. Invading bacteria and the chemical products of their activity are adequate stimuli to certain chemical ceptors. These mechanisms, when excited to intense activity as in infection, cause a breaking down of foreign protein molecules without breaking down the living protein molecules of the organism; and by this means the standard of chemical purity of the body is maintained in the presence of infection. This chemical defense gives rise to the principal phenomena of infection and auto-intoxication and will be discussed later.

In the response to local infection by *phagocytosis* and the response to general infection by processes of *immunity* we have recapitulations of phylogenetic associations of a vast antiquity.

Retracing our steps down the line of the animal kingdom, we note that the chief difference between animals and vegetables is the inability of the former to nourish themselves directly from the environmental media. Animals cannot transform the elements of inorganic salts into protein molecules, but must depend upon a previous synthesis and assimilation of those salts by plants or lower animals. This weakness is exhibited in the single-celled amœba and other protozoa by a major diet of bacteria, almost any species of which they will envelop and attempt to appropriate. Against this offensive activity on the part of the protozoa the bacteria have developed a counter self-defensive adaptation in the form of a poisonous secretion, which kills their enemy after it has devoured them. This war between "host" and "parasite,"

thus begun in the lowest forms of life, continues throughout all species of animals, and is waged perpetually with varying success for each participant. There occurs now the death of the "host," now the defeat of the "parasite"; and now, again, a mutual compromise — symbiosis — which is of benefit to both. There are many interesting examples of this constant warfare in the bodies of men and animals. In fact, infection is but an illustration in miniature of that great principle which is being demonstrated on a larger scale throughout all nature, namely, that it is not man alone, but all the world besides, which is undergoing "adaptation to environment."

Symbiosis and Parasitism

Out of these reciprocal adaptations of animals to plants, plants to other plants and animals to other animals result some of the most characteristic phenomena of life. Thus, the color, the shape and the nectar of flowers are undoubtedly determined by the physical forms and habits of the fertilizing insects which visit them. On the other hand, the proboscis of the insect, its wings and perhaps its sense of smell have, in turn, been evolved by the existence of the flower from which it gets its chief nourishment. The nectar of the flower supplies the insect with the required carbohydrate fuel to make its flight — that is, the flower furnishes the motor power, the "gasoline." These interrelations and interdependencies of one organism upon another become so firmly established, after a time, that to alter their *status quo* in any respect is often to alter the life equation for numerous organisms.

Thus Romanes mentions the extinction of white clover in Suffolk as a result of the destruction of cats. The plants were dependent for their fertilization upon the humble bees, whose nests fell a prey to the rapidly multiplying field mice which naturally profited by the destruction of their enemies, the cats. A similar disturbance was unexpectedly precipitated in Jamaica by the introduction of the Indian mongoose to destroy the cobra. In Jamaica, the mongoose, in addition to its natural prey, ate the eggs of the song birds. The decrease in the number of the birds immediately led to an increase of ticks, which preyed upon and destroyed the cattle, and even the mongoose itself. In some cases such reciprocal dependence of living creatures upon each other for life is so close, that they may be regarded as compound beings. Darwin cites many instances of these simultaneously evolved organisms among insectivorous plants. Other examples are the crocodile bird which subsists upon pickings from the teeth of the crocodile; and the rhinoceros bird which feeds upon insects buried in the hide of the rhinoceros, while, like the crocodile bird, it pays for its board by taking sudden flight at the approach of a stranger, thus warning its host of the proximity of danger.

If men and animals prey upon the vegetable world, the vegetable world in turn preys upon the animal world through the medium of microscopic life. The same co-adaptations that obtain among macroscopic organisms obtain also between them and their microscopic "parasites." And harmful as many of these adaptations are for man, when the trial balance is struck, they are, in the aggregate, of great benefit to

him. The fundamental action of bacterial life is the resolution of dead organic matter into its inorganic elements. Were animals and plants deprived of these natural scavengers, the earth's surface would soon be choked with an accumulation of the dead which would ultimately destroy all vegetable and animal life, including man himself.

There are many instances of beneficent bacteria without the body of man. Such, for instance, are the bacteria which assist in replenishing worn-out soil by absorbing nitrogen from the air and offering it in available form to the growing plants; the bacteria which accomplish the fermentation of wine, which ripen cheese and which put the flavor into butter, which tan hides and which cure tobacco. Within the body of man ample opportunity is provided for the useful domestication of bacteria by the quantities of dead matter and deleterious poisons constantly being thrown off by the living tissues. Wherever on or in the body there have constantly throughout phylogeny been found unresolved organic elements of food, of secretions or excretions, there are found also specific types of "parasitic" organisms evolved to utilize the débris which would otherwise have accumulated and hindered some important function. Thus we have bacteria which reside normally in the oily secretion of the skin, the waste matter of the intestines, the mucous secretions of the mouth, the nose, the throat, the lungs and the genital tract — our phylogenetic scullery maids.

Of all these scavengers the most useful and perhaps the least appreciated are the gaso-genetic bacteria,

one of which is the *colon bacillus*. By the production of gas these bacteria aid the peristaltic movements of the intestines and the movements of the diaphragm, in the acts of breathing, talking and vomiting for which resilient abdominal contents are necessary. On the other hand, it is probable that the bacteria themselves have had a selective influence on the modification of the intestines and abdomen — perhaps even of food itself — to meet their own life requirements. So intimate is this reciprocal relation that, like the insects and the flowering plants, like the rhinoceros and the rhinoceros bird, man and his gasogenetic bacteria form a strange partnership for mutual profit.

Disturbed Symbiosis and Disease

These symbiotic relations, normally so useful to man, may be easily disturbed and cause disease or "infection" — a triumphal adaptation for the bacteria at the expense of man. It is but a step for these bacterial residents from a temperate diet of cell secretion in time of health to an intemperate consumption of cell substance itself, when the resistance of the host is low. Thus the diphtheria bacilli, normally resident in the throat, may turn upon their cellular benefactors and run riot in *diphtheria*. Thus the pneumococci, constantly present in the pulmonary tract, may attack the source of their food supply and cause *pneumonia*. Thus the bacteria of the nose may attack its membrane, the secretion of which they subsist upon, and cause a cold; or the *colon bacilli*, normally resident in the intestine, may suddenly attack the peritoneum, when the condition of the appendix is such as to reduce its

local resistance, and may cause *appendicitis* and *peritonitis*. Thus, *syphilis* and *gonorrhea* may have originated from earlier harmless species of *spirochetæ* and *gonococci*, which at first subsisted normally upon the specific secretions of the genitalia, but later through adaptive changes became abnormal and harmful. Notable evidence of the adaptive origin of gonorrhea and syphilis is offered by Ehrlich in his observation that the spirochetæ grow best in a culture made from the testicles of the higher apes. It is also noteworthy that no corresponding diseases exist among animals which conjugate only at rutting time. To evolve a species of microörganism adapted to a certain food supply peculiar to one region of the body, would require, as a basis for that evolution, a constant, or nearly constant, supply of that food.

Phagocytosis

As the bacteria met the first adaptive attack of the amœba by evolving poisonous secretions, so the higher organism meets the attempt of bacteria to overcome its equilibrium by evolving substances which destroy or neutralize the power of the invaders. The most primitive type of these chemical defense mechanisms to be found in higher organisms is an exact analogy of the nutritive process by which the amœba envelops and digests the bacteria in its environment. This is the action of the *phagocytes*, amœboid-like bodies, which move from place to place in the organism and envelop and digest certain substances alien to the organism. The specific habitat of these peripatetic guardians is in the blood and the lymph. Because of

their power to digest waste matter in the body they were termed *phagocytes* by Metchnikoff, who first fully demonstrated their properties and who designated as *phagocytosis* the whole process by which certain bacteria, foreign materials and the dead tissues of the animal itself are destroyed.

The similarity of the process to unicellular digestion may be observed in a sponge or in the larva of the echinoderm. If a foreign substance be introduced into the body cavity of these organisms, cells analogous to the leucocytes of higher organisms collect around the invader and prevent its further progress by fusing into a hard plasmodial mass. The protecting cells then adhere to the invaders and gradually ingest and absorb them. This operation continues until every particle of dead matter has been absorbed, after which the protecting cells move away from the seat of injury, and the damage is repaired by normal cell proliferation. This action is in substance that which takes place in the human organism when the body is attacked by a local infection which gains entrance through an external wound. The live or dead organic substance serves as a stimulus by which the protective activity of the leucocytes is excited, first in the local area, and then, if this be insufficient, by calling out the reserve forces of leucocytes throughout the whole organism.

Immunity

For the common daily menaces of pyogenic infections, these phagocytic mechanisms are, in the main, adequate. But there are many infections which cannot be successfully met at the local point of entrance

by the phagocytes. Other types of chemical defense mechanisms, therefore, have been evolved to cope with these more generally disseminated dangers. Like the simpler process of leucocytosis, the action of these more complex chemical mechanisms shows a schematic resemblance to the process of digestion in its more highly evolved stages. In sponges and hydræ, for example, food is ingested by the individual cells lining the gastric cavity, the food particles being taken in directly, just as the leucocytes of the mammal take in foreign particles, or the amœba engulfs its food. In higher organisms this intra-cellular process of digestion has been succeeded by a process differentiated among a number of specialized cells lining the digestive tract, some of which secrete digestive ferments which in turn prepare the food for absorption. A similar modification seems to have taken place in the means adopted by the organism for its defense against infection. Thus, while certain of the leucocytes destroy bacteria by a process of intracellular digestion, other cells of the body seem to be excited by the invasion of certain other microörganisms to secrete into the surrounding body fluid chemical substances which act as poisons to the bacteria or as neutralizers of the poisonous secretions from the bacteria.

This production of anti-bodies is in every instance essentially a specific reaction excited by a specific chemical stimulus. That is, the anti-bodies produced in response to an invasion of diphtheria germs are specific for that microörganism and useless as a defense against the invasion of any other microbe. The antitoxin of cerebro-spinal meningitis is powerless to

neutralize the toxin of tuberculosis. The antitoxin of diphtheria is inactive against typhoid, erysipelas or pneumonia. As Ehrlich has picturesquely expressed it, the anti-bodies produced by the blood substance in response to infectious invasions are "charmed bullets" which strike only the objects against which they have been evolved as weapons by the organism.

Thus we see that the same law of natural selection, which has built up a system of contact ceptors in the skin for the defense of the body against gross material enemies, has evolved a system of chemical ceptors and specific chemical reactions for the apprehension and destruction of microscopic enemies within the organism. The same law of phylogenetic association, which is responsible for the muscular reaction of defense against physical injury, is responsible for the chemical defense against microörganisms, and against all foreign protein material whether from excessive protein food, pregnancy or infection. As a physical blow, light, heat, cold or tickling supplies the needed factor for the release of energy for physical defense through the excitation of contact ceptors, so the injection of live or dead bacteria or of foreign protein substance into the blood stream of the body supplies the exciting factor which calls out the activity of chemical defenses through the excitation of chemical ceptors. On this important fact is based the theory and practice of serum-therapy and of vaccination, by which diphtheria, typhoid, smallpox, tetanus and other diseases are conquered.

The physician who contemplates this identity of *noci association* in the infections with the *noci associations* of physical contact will call to mind many

facts of clinical experience which confirm the parallel evolution of the two. It is noticeable that just as natural selection has established *contact ceptors* only for those types of physical contact which the species experienced during its phylogeny, it has likewise established *chemical ceptors* only for those chemical substances which during phylogeny affected the existence of the organism. In this connection it is interesting to compare the physiological response of the organism to a dose of toxins with its response to a dose of a standard drug. There are no well-known drugs except the iodin compounds (analogous in chemical nature to thyroid extract) which cause a febrile response in the system, and there is no drug which causes a chill. On the other hand, all the specific toxins cause febrile responses, and many cause chills. Had man's progenitors been poisoned by a given drug throughout the evolution of the species, natural selection would have eliminated those individuals unable to evolve a specific response to that drug and a self-defensive mechanism against it. The administration of the drug would then cause a *noci association* with a consequent reaction analogous to the reaction which follows the injection of toxins.

The inaugural symptoms of most infections reproduce in miniature all the typical phenomena of the ensuing disease, just as by rapid pulse, increased respiration, trembling, pallor and muscular weakness the phenomena of fear or of anger recapitulate all the physiological phenomena which accompany the flight from an enemy or the physical combat of which they are the precursors. In the dullness, stupor, headache,

and loss of appetite which inaugurate typhoid, we have a picture of the long, slow course of the disease which involves the digestive apparatus and exhausts the system. In the thickened voice, the difficult breathing and the abrupt high rise in temperature in diphtheria, in the activated *alæ nasi*, the rapid respiration and the high fever of pneumonia, we have brief summaries of the quick and desperate combats with infection which are waged between host and invader before victory is declared for one or the other.

Undoubtedly, each move in these fast and furious struggles, or slow sieges, between man and his microscopic enemies is typical of the long and strenuous biologic contest which has gone on for ages between the two adapting organisms — the host and the invader — *umpired impartially by natural selection.* It is reasonable to believe that every advance of the human organism toward immunity has been met by a like advance on the part of the microörganism toward a more effectual attack and resistance. This is evidenced by the increased vitality of certain specific microörganisms which survive a curative dose of mercury or arsenic in the system. It was noticed by Ehrlich that a large initial dose of the specific drug is of more value in destroying the spirochetæ than a series of minor injections, which are lessened in efficiency by reason of the fact that portions of the culture which survive the first dose become adapted to withstand a larger dose. The desperate struggle of the organism in acute infection bears testimony to the fact that the rules of fight for these encounters have been firmly established and standardized. Man and the acute

infections are old enemies. Organisms strange to each other have no rules for fight. This is evidenced by the high mortality which results from the introduction of infections into countries in which they are not indigenous, so that natural selection has had no opportunity to protect the organism by a long series of selective struggles. When measles was first introduced into Samoa by Europeans, it wrought a cruel havoc among the natives. When *la grippe* was first imported into Russia, it ran a severe course. In like manner, many of the terrible epidemics of "plague" in ancient history may have been due to the appearance of some new germ or the spasmodic rehabilitation of an old one.

Distribution of Chemical Ceptors

The same relation which exists between contact ceptors and their distribution in those parts of the organism, where harm-producing agents would have been encountered throughout its evolution, exists between chemical ceptors and the parts of the body most commonly exposed to the local invasion of infectious agents. Many of these areas, such as the skin surface and the superficial organs, are identical with the pain areas, but many other parts of the body, which are totally devoid of the contact ceptors, are abundantly provided with chemical ceptors for the apprehension of their own specific menaces. The surfaces of the face, the neck and scalp, the extremities, the eyes, the nose, the throat and the lungs, which have constantly been exposed to pyogenic infections, are, as one would expect, well equipped with protective mechanisms. The lungs, which make no re-

sponse to perforation by an external agent, respond actively to the invasion of pneumococci, since these are ancient enemies. The peritoneum, which throughout phylogeny has been exposed to infection through the genital tract and through the intestinal walls, has an efficient mechanism for overcoming infection, but makes no response when it is cut or burned.

On the other hand, the brain and the lining of the heart which have been protected as securely against pyogenic invasion as from physical impacts are helpless in the face of infection, as the external areas are helpless before the X-ray. Once lodged in either the brain or the heart, infection works its way painlessly and persistently, undeterred by a local resistance. The same inability to cope with the infrequent invader marks all deep-seated areas which have had no open connection with the outside world. Thus below the surface of the face, neck, chest and abdomen, we find that the power of resistance to infection diminishes as the depth of the tissue below the surface increases. The great vascular trunks buried deep in the chest and abdomen show little resistance to infection, although curiously enough, when they emerge to more exposed positions in the thigh and leg, they react to infection by swelling, pain and other symptoms of inflammation, as do other tissues which have been frequently subjected to infection from open wounds. The mediastinum has practically no mechanism of defense against infection. An abscess may progress unheralded in the space between the diaphragm and the liver, in the retroperitoneal region, in the mediastinum, in the pericar-

dium, in the liver, in the brain — none of which has evolved a chemical mechanism for defense.

But what of the peritoneum itself, and of the organs whose functions compel them to maintain communication with the outer environment? Certainly the peritoneum has been constantly exposed to infection from without through perforation, as well as to infection from the intestines, and should have evolved an effective protective mechanism. Nothing could offer more striking evidence of the fact that it has done so than the phenomena which ensue when the peritoneum is infected. These phenomena are a quick, local discharge of free fluid laden with opsonins; the formation of an adhesive exudation; the arrest of the peristaltic movements, in order to prevent a further spread of the infection; pain, incidental to the fixation of muscles for the same purpose; loss of appetite, to prevent the intake of more food; vomiting, to rid the stomach and the upper portion of the intestines from decomposing contents, which the inhibitory stasis has caused to accumulate — the entire complex response being effected through chemical ceptor stimulation.

The successful defiance of infection by the genito-urinary tract is well known. Here the uterus, vagina and fallopian tubes keep constantly open a dangerous passage-way to an environment laden with infection. The gall bladder and bile ducts and the pancreatic ducts connect directly with the intestinal field which teems with infection. Yet through selection and adaptation all these organs have become qualified to maintain freedom from infection under normal conditions. But if injury to the lining of any of these

tracts lowers the local resistance, infection is at once inaugurated. Moreover, it is in the pelvis that the defense mechanism of the peritoneum against infection is most marked, being more efficient here than in higher portions. This is the natural sequence of the many hazards which have been encountered in the pelvis, not alone from the accidents of childbirth, but from the proximity of the fallopian tubes and the appendix, infections of which always must have been communicated to the pelvic peritoneum. In this connection the evolution of the omentum is of especial interest. Just long enough to reach to the bottom of the pelvis, apparently its only use is to move toward, envelop and localize an infected point, thus serving as a most valuable guardian to the whole abdominal cavity. In its perfect altruism, the omentum may fittingly be termed the philanthropist of the abdomen.

In many other parts of the organism, and in many pathologic conditions, we have convincing evidence of the establishment, through natural selection, of certain specific chemical reactions adapted to the biologic needs of the organism, which are equally remarkable examples of its inherent ability to right itself automatically when threatened by a menace from an inner or outer environment.

These specific chemical reactions, of which blood coagulation and immunity against infection are among the best known and most adequate, differ from ordinary chemical reactions by reason of what seems to be a kind of opportune team-work between isolated chemical substances evolved through natural selection. These substances lie dormant in different parts of the

body, awaiting the arrival of the special contingency which provides the stimulus for their interaction. Such are anti-bodies, the digestive agents and the constituents which cause blood clotting, each of which justifies its presence in the body by the specific protective activity it manifests in the face of the specific contingency as a result of which it was evolved.

Mechanism of Blood Coagulation

The mechanism of blood coagulation is of vital interest in this connection. The blood must be maintained in perfect fluid form within the uninjured vessel, but any opening must be immediately covered, for if the flow of blood could not be stemmed by clotting, the slightest cut and many normal functional processes would result in death as a result of unopposed hemorrhage.

Normally, the blood contains all the constituents necessary for coagulation, and in addition it contains an antagonistic element, known as anti-thrombin, which inhibits intravascular coagulation. A neutralizing agent for anti-thrombin — thromboplastin (Howell) — is contained in the adjacent tissues and in the outer layers of the walls of the blood vessels themselves. When a blood vessel is cut or torn, thromboplastin comes in contact with and neutralizes antithrombin — causing immediate clotting.

It is obvious that intravascular coagulation would be a more certain method of arresting hemorrhage; but intravascular coagulation would involve the danger of embolism and the danger of clotting where there is [illegible] hemorrhage. To meet cases of extreme danger

there has been evolved an additional method of arresting hemorrhage by a rapid increase in the coagulation of the blood when the blood-pressure is low; for example, just before death from hemorrhage the blood current is feeble, and the clots are not easily carried away.

Low blood-pressure produces anemia of the brain, which in turn occasions fainting; thus fainting occurs in connection with great loss of blood. Indeed it is probable that fainting and hemorrhage have had a simultaneous biologic origin. It is a common tendency of both men and women — of women rather than men — to faint at the sight of blood. Women have always been exposed to the disastrous hemorrhage of childbirth, and therefore, more than men, have needed the salutary reaction of a low blood-pressure to arrest the bleeding. Acting on this assumption, I have clinically utilized the fainting point as a remedy against internal hemorrhage. Patients with internal hemorrhage are propped upright in bed, or the blood is segregated in the limbs in such a manner that the patient is constantly on the verge of fainting. This procedure, persisted in for some time, has in three instances adequately arrested internal hemorrhage. As soon as the hemorrhage has ceased, the patient is allowed to lie down, and adequate circulation through the brain is restored. Fainting never occurs in the course of acute infections, such as peritonitis, osteo-myelitis or typhoid fever. It may occur as a result of strong emotion, but its most common incentive is the telltale sight of blood. Its phylogenetic origin, therefore, was apparently associated with bleeding.

If the mechanism of blood coagulation was evolved through the biologic exigency of hemorrhage, usually from wounds received in combat, then according to the law of phylogenetic association, we should conclude that the *areas most exposed phylogenetically to injury would be more fully equipped with the elements for coagulation than the more protected regions.* In other words, we should expect to find that the inner parts, less frequently subject to laceration, would show a higher tendency to protracted hemorrhage than do the commonly exposed areas of the surface and the extremities. Clinically, we know that in general this is true; that the quick coagulation of blood in the superficial tissues — skin, subcutaneous tissues and muscles — is in sharp contrast to the slow coagulation in the protected fields. The mucous membrane of the frequently wounded mouth bleeds slowly and heals quickly. On the other hand, the mucous membranes of the stomach and intestines, of the bladder, of the fallopian tubes and of the respiratory tract show a tendency to bleed indefinitely. Limbs may be crushed and torn, evulsed even, with less hemorrhage than is caused by a slight abrasion of the mucous membrane of the intestines.

It may be argued that the quick coagulation in external tissues is due to contact with oxygen. How, then, would one account for the fact that bleeding in subcutaneous wounds, where there is no supply of oxygen, is arrested with equal promptness? The extensive laceration of blood-vessels in childbirth is quickly overcome, whereas nose-bleed, with all the advantages of air contact, may persist stubbornly, and operations on the tonsil, where there is an ample supply of air,

are often attended by persistent bleeding, while an equally extensive incision and laceration of the tissues of the mouth results in little inconvenience from bleeding. The persistent bleeding of the lungs in pulmonary tuberculosis is well known and is in accord with the meager phylogenetic experience of this area with trauma. Interesting and relevant is the discovery of Sir Victor Horsley that a bit of raw muscle taken from an external part and applied to a bleeding point will quickly arrest hemorrhage. Of interest also is Cannon's discovery that the blood of animals in rage shows a higher tendency to coagulate. Rage is the natural accompaniment of combat, which in turn is the biologic setting for laceration and bleeding. Animals in rage show an increased secretion of adrenin; and adrenin, according to Cannon, increases the tendency of the blood to coagulate.

A further adaptation favorable to blood clotting in a lacerated blood vessel is to be seen in the disposition of the slender strands of connective tissue fibers which form the outer layer of the blood-vessel wall. Injury to the vessel causes these tiny fibers to be thrown athwart the rent in a tangled meshwork, interfering with the flow of the blood and constituting the foreign substance which always facilitates the chemical act of coagulation.

If coagulation be precipitated by thromboplastin (Howell), then one ought to find an uneven distribution of thromboplastin in the various tissues of the body corresponding to the variations in the coagulation times in those parts. This point was partially tested in a research in my laboratory by means of Howell's

method, using extracts of tissues taken from those parts of the body, which, clinically, show differences in the coagulation times. In these experiments tissues were taken from the brain, the skin, the skeletal muscles, the buccal mucous membrane, the lungs, the pancreas, the deep lumbar muscles, the heart muscle, the intestinal mucosa, the thyroid and the kidney. Although the data are insufficient to be conclusive, the results recorded are in keeping with clinical observations. That is, the quantity of thromboplastin in the skin and in the muscles was, in general, greater than in the pancreas, the deep lumbar muscles and the intestinal mucosa. These facts point to the conclusion that the distribution of thromboplastin throughout the body, like the distribution of *contact ceptors* and of the *mechanisms* for *combating pyogenic infection*, has been determined by the past experience of the species and by the relentless laws governing the survival of the fittest.

Acidity and Respiration

Among other chemical mechanisms which have been evolved for a specific purpose are the cerebral mechanisms for the maintenance of the normal alkalinity of the blood and the chemical purity of the body. The most important receptor mechanism for the maintenance of the normal alkalescence is the respiratory center in the medulla, which is governed by the H-ion concentration[1] and possibly in part by the oxygen content

[1] The alkalinity or acidity of a fluid depends upon the number of free OH or H-ions it contains, — an ion being an electrical molecule. The degree of acidity of a fluid, therefore, may be determined by measuring the hydrogen ions it contains, *i.e.*, its H-ion concentration.

of the blood. Increase in the H-ion concentration of the blood *stimulates* the respiratory center and, simultaneously, *inhibits* the cortical or driving portion of the brain. In part, increased H-ion concentration is produced by the driving action of the higher brain centers, the acidity being in part overcome by carbon dioxid elimination in respiration. Other important acid-reducing factors will be noted later. Hence, we find an antithetic or balanced reaction between the cortex and the medulla as a result of changes in H-ion concentration; *the cortex increasing the production of acidity, the medulla decreasing it by increasing acid neutralization.* Thus, in the midst of an activating environment, the normal alkalescence is maintained.

There is evidence also that there exists in the brain a mechanism which activates the organs of the kinetic system[1] to the end that the chemical purity of the body may be maintained when *foreign proteins* are present, exactly as the same organs are driven in response to *contact and distance ceptor* stimulation. These points will be taken up later.

[1] See Chapter VI, *The Kinetic System.*

CHAPTER V

ADAPTATION BY MEANS OF DISTANCE CEPTORS — EMOTIONS — MENTAL STATES

ADAPTATION to environment in some species of animals, such as the oyster, is secured mainly by reactions to stimulation of the contact and chemical ceptors only; but in most animals there has been evolved a third method of adaptation to environment by which they are directed toward beneficial objects in their *distant* environment and away from those that are harmful, thus securing a quicker and surer adjustment than would be possible through contact and chemical ceptors only.

The essential difference between the reactions initiated by stimulation of the distance ceptors and those initiated by stimulation of the contact ceptors lies in the fact that in the response to distance ceptor stimulation the animal *as a whole* responds, while in the response to contact ceptor stimulation, usually only a portion of the organism is concerned; consequently the transformation of potential into kinetic energy for the consummation of the response to distance ceptor stimulation is much greater than in the response to contact ceptor stimulation. Stimulation of the distance ceptors initiates the long series of motor acts connected with the search and fight for food and mates; the grappling with enemies or fleeing from them. It

is by means of distance ceptor stimulation that most herd and community adaptations are affected — adaptations which were evolved, as Sherrington and others have shown, simultaneously with the power of locomotion.

Integration of the animal is achieved no less by the inhibition of these locomotor acts than by the consummation of them. A dog standing rigid and alert pointing game; a cat stalking a bird; or a hare fleeing before hounds, is each in like manner activated through its distance ceptors to assume a posture or a series of postures of the body, in which not one but all parts of the skeletal musculature are concerned. Whether it be to impel locomotion or to cut it short, therefore, the animal *as a whole* is activated through the stimulation of its distance ceptors.

As there is no break in the automatic continuity of action between the incidence of the adequate stimulus for a muscular reflex and the production of a protective motor act specific to that stimulus, so there is no break between the incidence of the environmental stimulus upon the distance ceptors and the motor activity which is the end effect of that stimulus. The flight of the giant water buffalo at the sight of a lion, or the charge of the lion at the sight of its prey, is as automatic a reaction as is the withdrawal of the limb of a rabbit from the sharp prick of a thorn. The delicate recording mechanisms of the eye, the ear and the nose, which were evolved to receive and transmit to the brain the specific impulses of a certain range of light waves, of sound waves and of material emanations, meet in the brain other mechanisms equally delicate and labile.

The labile mechanisms in the brain transform some of their energy into nerve impulses, which in turn excite or inhibit the activity of certain muscles; or, even if muscular activity does not result, the glands whose activity assists in the adaptive response of muscular action in running or fighting are stimulated, while other glands not useful in such action are inhibited. For each adequate stimulus in the environment there is postulated, as we have already stated in a preceding chapter, a facilitated path or mechanism of action, — "facilitated" through natural selection, — a mechanism consisting of receptor, conductor and effector paths, and for convenience designated an *action pattern*.

Thus, by infinitesimal changes in the length of light waves are produced chemical and physical changes in the rods and cones of the eye, as a result of which variations in color are perceived. Thus slight variations in light waves result in the perception of one animal by another and become the adaptive stimuli which excite the action pattern of fighting or of flight. In like manner are excited the infinite number of action patterns by which man responds adaptively to environment. As in the case of the muscular reflex, the occurrence of the adequate stimulus acts like the pressing of a button connected with a mechanism by means of which a store of potential energy is converted into kinetic energy in accordance with the phylogenetic import of the exciting stimulus.

There are many facts which support this postulate, notable among which are the anatomy of the eye and the chemical and histologic changes which take place in that organ; the specificity of response and the

modification of the response through experience and heredity; the evidence of histologic changes found in the brain cells after response has been effected, and in the eye which has been exhausted by intense light; the fact that electric energy is generated in the nerve centers and flows along the nerve paths; the fact that the response of muscles and glands to an electric current is the same as their response to a nerve impulse; and the conclusion of Crehore and Williams,[1] that the propagation of nerve impulses obeys the laws of the propagation of electricity along conductors with distributed capacity. All these points will be considered later. The point which concerns us here is the fact that the response to distance ceptor stimulation is *specific* to the exciting stimulus, just as are the responses to contact and chemical ceptor stimulation; and that like the latter they serve a useful purpose in the life of the species. The evidences of this are the gross phenomena, the physiological modifications, and the histological and chemical changes which are produced in the cells of certain organs in the reactions to distance ceptor stimulation, all of which show that in these reactions, whether they are manifested by muscular activity, by inhibition of muscular activity or by emotion, the entire organism is integrated to perform a physical act of muscular exertion, indistinguishable from the motor acts of self-defense and species preservation.

Muscular exertion is produced for three principal

[1] Crehore and Williams: Electric current in conductors with distributed capacity — considered in relation to the propagation of the nerve impulse. Proceedings of the Society for Experimental Biology and Medicine, 1914, XI, pp. 58–59.

purposes: for defense, for procuring food, and for accomplishing procreation. Reduced to its lowest terms, each one of the reactions concerned with these purposes may be represented by some form of motor or chemical activity.

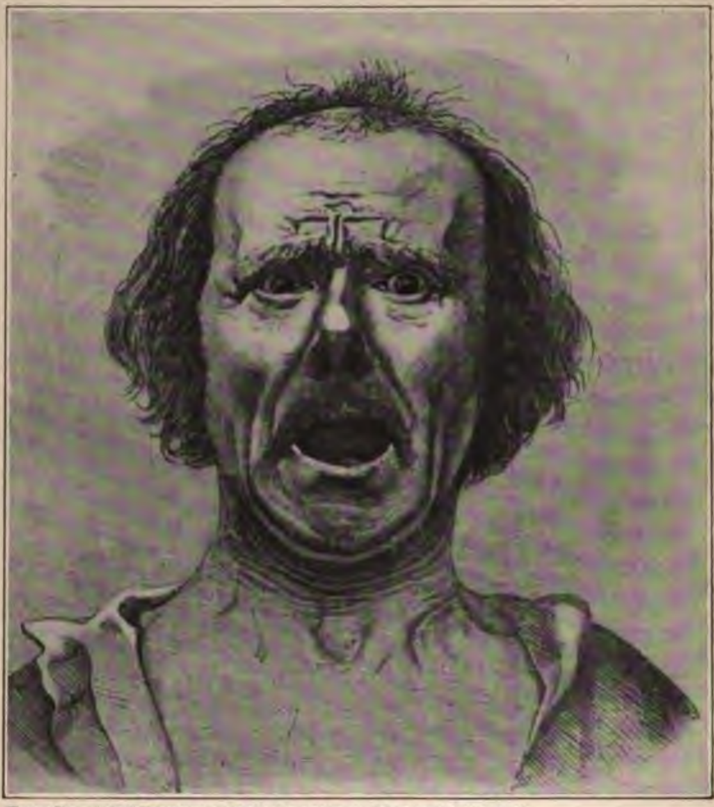
Emotion a Form of Muscular Activation

The resemblance between emotion and muscular exertion was first pointed out many years ago by Darwin and other evolutionists who have given remarkably accurate and vivid descriptions of the outward expressions of both major and minor emotions, showing their likeness to the acts of flight, combat or embrace; and postulating that their origin was simultaneous with the biologic necessities of escaping from injury, securing prey and accomplishing procreation; and that, like language, play, song, music, etc., they were evolved as highly advantageous means of expediting these motor processes. In his book, "The Expression of the Emotions in Men and Animals," Darwin gives the following description of fear and terror:

"Fear is often preceded by astonishment, and is so far akin to it, that both lead to the senses of sight and hearing being instantly aroused. In both cases the eyes and mouth are widely opened, and the eyebrows raised. The frightened man at first stands like a statue motionless and breathless, or crouches down as if instinctively to escape observation. The heart beats quickly and violently, so that it palpitates or knocks against the ribs. . . . That the skin is much affected under the sense of great fear, we see in the marvellous and inexplicable manner in which

perspiration immediately exudes from it. This exudation is all the more remarkable, as the surface is then cold, and hence the term a cold sweat; whereas, the sudorific glands are properly excited into action when the surface is heated. The hairs also on the skin stand erect; and the superficial muscles shiver. In connection with the disturbed action of the heart, the breathing is hurried. The salivary glands act imperfectly; the mouth becomes dry, and is often opened and shut. I have also noticed that under slight fear there is a strong tendency to yawn. One of the best marked symptoms is the trembling of all the muscles of the body; and this is often first seen in the lips. From this cause, and from the dryness of the mouth, the voice becomes husky and indistinct, or may altogether fail. . . . As fear increases into agony of terror, we behold, as under all violent emotions, diversified results. The heart beats wildly, or may fail to act and faintness ensue; there is a deathlike pallor; the breathing is labored; the wings of the nostrils are widely dilated; 'there is a gasping and convulsive motion of the lips, a tremor on the hollow cheek, a gulping and catching of the throat;' the uncovered and protruding eyeballs are fixed on the object of terror; or they may roll restlessly from side to side. . . . The pupils are said to be enormously dilated. All the muscles of the body may become rigid, or may be thrown into convulsive movements. The hands are alternately clenched and opened, often with a twitching movement. The arms may be protruded, as if to avert some dreadful danger, or may be thrown widely over the head. . . . In other cases there is

a sudden and uncontrollable tendency to headlong flight; and so strong is this, that the boldest soldiers may be seized with a sudden panic. As fear rises to an extreme pitch, the dreadful scream of terror is



From Darwin's "Expression of the Emotions in Men and Animals."

FIG. 7.—HORROR AND AGONY.

heard. Great beads of sweat stand on the skin. All the muscles of the body are relaxed. Utter prostration soon follows, and the mental powers fail. The intestines are affected. The sphincter muscles cease

to act and no longer retain the contents of the body. . . . Men, during numberless generations, have endeavored to escape from their enemies or danger by headlong flight, or by violently struggling with them; and such great exertions will have caused the heart to beat rapidly, the breathing to be hurried, the chest to heave, and the nostrils to be dilated. As these exertions have often been prolonged to the last extremity, the final result will have been utter prostration, pallor, perspiration, trembling of all the muscles, or their complete relaxation. And now, whenever the emotion of fear is strongly felt, though it may not lead to any exertion, the same results tend to reappear, through the force of inheritance and association." (Fig. 7.)

Phylogenetic Origin of Emotions

That fear had its phylogenetic origin in the motor activity of efforts to escape from injury is the conclusion also of Herbert Spencer, who in his "Principles of Psychology" says: "Fear, when strong, expresses itself in cries, in efforts to escape, in palpitations, in tremblings, and these are just the manifestations that go along with an actual suffering of the evil feared. The destructive passion is shown in a general tension of the muscular system; in gnashing of the teeth and protrusion of the claws; in dilated eyes and nostrils; in growls; — and these are weaker forms of the actions that accompany the killing of prey."

This likeness of the gross phenomena of fear and rage to muscular activity is further substantiated by comparing the aspect of men and animals in the grip of

Photo by Paul Thompson.

FIG. 8. — ATHLETE MAKING A RECORD BROAD JUMP.

Activation for supreme physical exertion is wonderfully portrayed in this figure of an athlete making a record jump. Compare the facial expression with that of anger or fear.

strong emotion with that of individuals during supreme physical exertion when fighting, running, jumping or seizing prey. (Fig. 8.) The accompanying photographs of athletes during or immediately after

Photo by Paul Thompson.

FIG. 9. — FINISH OF ONE-HALF MILE INTERCOLLEGIATE RACE.

The last stage of exhaustion after extreme physical exertion is well portrayed by the two foremost runners.

the strenuous exertion of running and jumping (Fig. 9); the pictures of animals attacking and seizing prey; and the pictures of animals and men integrated by various emotions graphically portray

Photo by Paul Thompson.

FIG. 10. — ATHLETE BREAKING THE RECORD FOR SHOT PUT.

Supreme activation for immediate exertion is splendidly illustrated here. Contrast the expression of this athlete with those of the exhausted runners in Fig. 9.

Photo by A. S. Rudland & Sons.

FIG. 11. — ANGER IN MALE GORILLA.

this likeness (Figs. 10 and 11). Clinically, we know that extreme muscular tension, increased heart beat and respiration, profuse perspiration, staring eyes, dilated nostrils, pallor and trembling of the limbs, are

K

Photo by Brown Brothers, N. Y.

FIG. 12. — EXHAUSTED SUFFRAGIST.

The end-effects of both emotion and physical exertion are apparent in the pallor, the staring eyes, the dilated nostrils and the relaxed muscles of the mouth.

Darwin's "Expression of the Emotions in Man and Animals." (From life by Mr. Wood.)

Fig. 13. — Cat Terrified by Dog.

Note the crouching position, the arched back, the erect hair, and ears drawn closely back, the bared teeth and lifted paw — every muscle tense and ready for spring and attack.

as characteristic of fatigue and exhaustion from emotion as they are of fatigue and exhaustion from muscular exertion.

The expression and attitude of the activated and exhausted Marathon runner differ little from those of individuals overcome by terror or grief; or from the expression of exhaustion portrayed in the picture of the English suffragist who has undergone both psychic and physical activation to the utmost in her struggle for a moral cause. (Fig. 12.) Were only the faces of these persons seen, it would be difficult in many cases to determine whether they were making extreme physical exertion, experiencing pain or under the domination of anger or hate. The tense rigidity of the muscles of the face, the almost inevitable showing of the teeth and fixing of the jaws and the contortion of the body are alike in all.

Moreover, there is a striking similarity between the attitude and the expression of the individual activated by horror and the frightened cat, with its back hunched rigidly in apprehension of the attack of a dog (Fig. 13); between the athlete making his supreme effort and the eagerness of the leopard stalking its prey through the forest. There is little in the picture of the exhausted runner or in that of the woman prostrated by grief to indicate that in one case the exhaustion is "physical" and in the other "mental."

It is interesting also to contrast these pictures of individuals exhausted by extreme mental and physical activation with those of animals and men in a placid state of both mind and body. (Figs. 14 and 15.) Contrast, for instance, the rigidity and muscular tenseness of the lion attacking its prey, its claws imbedded in the thick muscles of the neck and back of its victim, with the soft, sensuous attitude of the tigress caress-

Photo by Underwood and Underwood, N.Y.

FIG. 14. — VIOLENT EFFORT.

Photograph of the head of a runner, sculptured from life by Dr. R. Tait McKenzie of the University of Pennsylvania, after a careful study of athletes in moments of supreme exertion.

Photo by Underwood and Underwood, N. Y.

FIG. 15. — EXHAUSTION.

Photograph of the head of an athlete, sculptured from life by Dr. R. Tait McKenzie of the University of Pennsylvania.

From Brehm's "Life of Animals."

FIG. 16. — TIGRESS AND CUBS AT REST.

Contrast the flexuous relaxed attitudes of this group with the tense and contorted appearance of animals and athletes activated by extreme physical exertion or emotion.

ing her cubs in the quiet shelter of her lair. (Fig. 16.) Contrast the contortion of the faces of the athletes with the composure of the beautiful woman posing for her portrait, and activated, we may believe, by no more stimulating concept than that of satisfaction with her beauty. (Fig. 17.) Contrast, as has Darwin, the rigidly hostile attitude of the dog approaching a stranger or an enemy with the fawning attitude of the same dog approaching its beloved master. Contrast these expressions of emotion and lack of emotion and see if they do not strongly suggest that emotion is as definitely a form of muscular activation as are the acts of escape, of seizure or of embrace.

Further striking evidence of the truth of this assumption is afforded by the fact that fear is experienced only by animals which depend for self-defense and species-preservation upon a swift locomotor reaction. The skunk, for example, whose chief means of protection is its odor; the porcupine, defended by its quills; the snake which repels its enemies by its venom; the turtle which is securely incased in its shell; the lion and the elephant secure in their superior strength — exhibit little if any fear. On the other hand, the rabbit, the bird, the deer, the horse, the antelope, the monkey and man — species which have ever had to struggle for existence against stronger or swifter enemies — these are the animals which preëminently exhibit fear and an irrepressible desire to flee from danger.

Physiological Phenomena of Emotion

The physiological phenomena exhibited by the organism stimulated to supreme physical exertion through a

FIG. 17. — COMPOSURE.

Contrast the impassiveness in the expression of this woman posing for her portrait with the contorted features of athletes, animals and men under muscular or emotional stress.

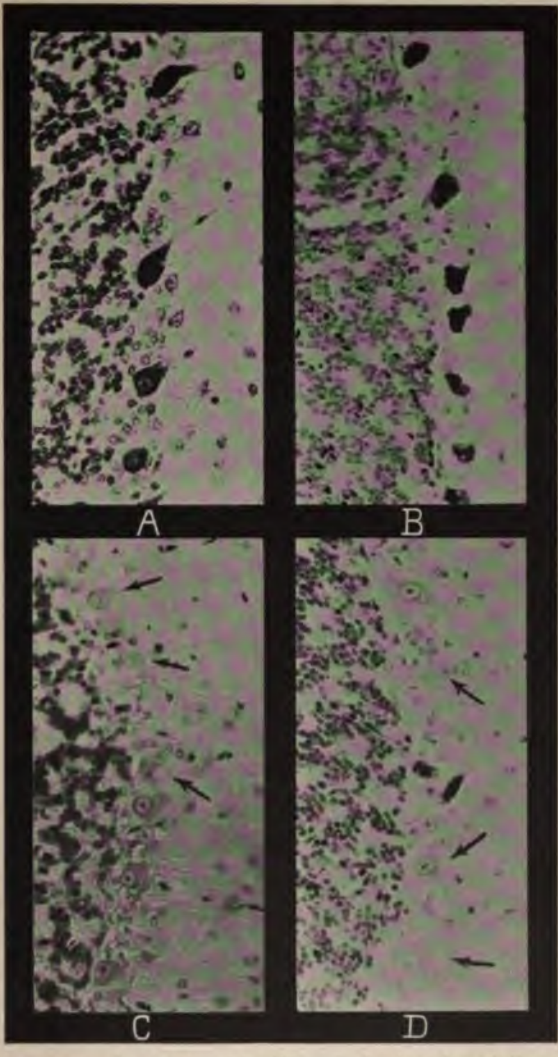
voluntary impulse, and the organism experiencing fear or rage are identical. The Marathon runner, like the rabbit terrified by a dog, exhibits the phenomena of increased blood-pressure and heart action, increased respiration, rising temperature, profuse perspiration, staring eyes, trembling limbs; and if the activation be sufficiently prolonged, muscular relaxation, dry mouth, pallor, indigestion, prostration and finally the collapse of every function.

Further evidence of the identity of the muscular activation in emotion and in physical exertion is found in a study of the physiological and histological changes caused by each. We have found also that intense emotion causes increased H-ion concentration in the blood, cerebrospinal fluid and urine.[1]

Histological Phenomena of Emotion

If the emotions are expressions of motor activity, which is itself dependent upon the driving power of the brain, one would expect to find that emotion produces histologic changes in the brain-cells identical with those produced by physical exertion. To test this point, animals were subjected to acute fear and to rage, some being killed immediately, others after varying intervals of rest. In those killed immediately, the brain-cells showed an increase of Nissl substance and of the percentage of active cells; while the brain-cells of animals which had been allowed varying periods of rest showed uniformly a loss of Nissl substance, the percentage of active cells being decreased

[1] Drs. Menten, Rogers, Harrison and Crozier.



A. Section of normal cerebellum of rabbit. B. Section of cerebellum of rabbit killed immediately after 25 minutes of fright. C. Section of cerebellum of rabbit after 40 minutes of fright, killed after 2½ hours of rest. D. Section of cerebellum of rabbit frightened twice a day for two weeks.

FIG. 18.—EFFECT OF FRIGHT, ACUTE AND CHRONIC, ON THE BRAIN-CELLS OF A RABBIT.

In B, the first effect of fright is seen in the hyperchromatic condition of the Purkinje cells to meet the increased demand of an emergency; this condition being followed by chromatolysis or disappearance of Nissl substance, as is evident in the cells of C. In D, the lasting effects of repeated fright are seen in the high percentage of fatigued and exhausted cells.

and the percentage of fatigued and exhausted cells increased. (Fig. 18.) The brain-cell changes wrought by emotion were identical with those wrought by running, by fighting, by infection, by auto-intoxication, by physical injury. In intense emotion some cells were destroyed, their number being proportional to the intensity and duration of the emotion. The cells modified by the emotions, but not destroyed, were restored to the normal state during sleep.

Having established the histologic evidence that "work" changes are produced in the brain by emotion, it is necessary to identify the organs the driving of which exhausts the brain-cells. The two organs whose secretions are known to increase most markedly the activity of the body are the thyroid and the adrenals.

Relation of the Thyroid to Distance Ceptor Stimulation

Fortunately a vast number of clinical observations shows a direct relation between the thyroid gland and the emotions. In acute emotions — fear, anger and sexual love — the thyroid gland frequently enlarges and becomes more vascular.

Beebe as well as Aschoff has shown that electrical stimulation of the nerve supply of the thyroid results in a diminution of the iodin content. It is known that the function of the thyroid is dependent upon the presence of iodin in combination with protein in the colloid material of the gland, from which it is probably mobilized by activating stimuli.

Why may this change in iodin content be regarded as evidence that the thyroid is activated by fear? Because the only proved function of the thyroid is the *metab-*

olism and *storage* of iodin in a protein combination. Iodized protein injected in excess into a normal animal causes most of the symptoms of fear — palpitation of the heart, rapid respiration, sweating, trembling, emaciation, inhibition of digestion, staring eyes, widened pupils, increased metabolism. Iodized protein causes changes in the brain-cells identical with the changes wrought by emotion. Like emotion, it causes also a lowered sugar tolerance and a tendency to glycosuria.

The thyroid gland has been called the organ of the emotions. It is the only gland in the body whose enlargement forms an essential factor of the disease *exophthalmic goiter*, whose phenomena resemble closely those of emotion. (Fig. 19.) Exophthalmic goiter, emotion and the excessive administration of iodin cause nearly identical phenomena. Excessive administration of iodin often causes a pathologic emotional state which cannot be distinguished from Graves' disease, and in continued overdosage, *iodin may even cause Graves' disease.*

What rôle may iodin play in the acceleration of body activities in emotion? The salient features of emotion, and also of that emotional disease, exophthalmic goiter, is a *lowered threshold to all stimuli,* whether of the contact, distance or chemical ceptors. The organism responds at such times to the prick of a pin, a hint of danger, or the slightest infection, by a transformation of energy many times greater than would follow the same stimulation in the normal organism. The researches of Osterhaut bear significantly upon this point and would seem to be of fundamental impor-

FIG. 19. — CASE OF EXOPHTHALMIC GOITER.

The identity of the mechanism stimulated by physical exertion, by emotion and by that emotional disease, *exophthalmic goiter*, is suggested by the facies of this typical patient. The *Graves'* patient is physiologically in a chronic state of activation for flight.

tance in interpreting both the emotions and Graves' disease. He has found that the addition of iodin to water in which kelp had been immersed facilitates the passage of electrical currents through the semi-permeable membranes surrounding the component cells of the kelp.

We have now three significant points for consideration: namely, that the thyroid fabricates and stores iodized protein; that during emotion iodized protein is *probably* thrown out of the gland in abnormal amounts; and that the effect of iodin is to decrease the resistance to the passage of electrical currents through semi-permeable membranes. The biologic deduction to be drawn from these facts is that in anger, fear and sexual love it is probable that the adequate stimulus reaches the brain and there causes the conversion of highly labile compounds into electric or some other form of transmissible energy, which passes on to stimulate the thyroid and other organs. The thyroid, being stimulated, throws iodized proteins into the circulation. The iodized proteins, reaching certain semi-permeable membranes, diminish the resistance to the activating current, thereby lowering the threshold to the specific stimulus and making more effective the specific response evoked by the stimulus, as a result of an increased sensitization of the whole effector mechanism. This sensitized or iodized state of the organism in turn facilitates a correspondingly increased driving by the brain of every organ and tissue in the body, with a total increase of energy transformation, which results in fatigue or exhaustion, according to the duration of the activation.

Relation of the Adrenals to Distance Ceptor Stimulation

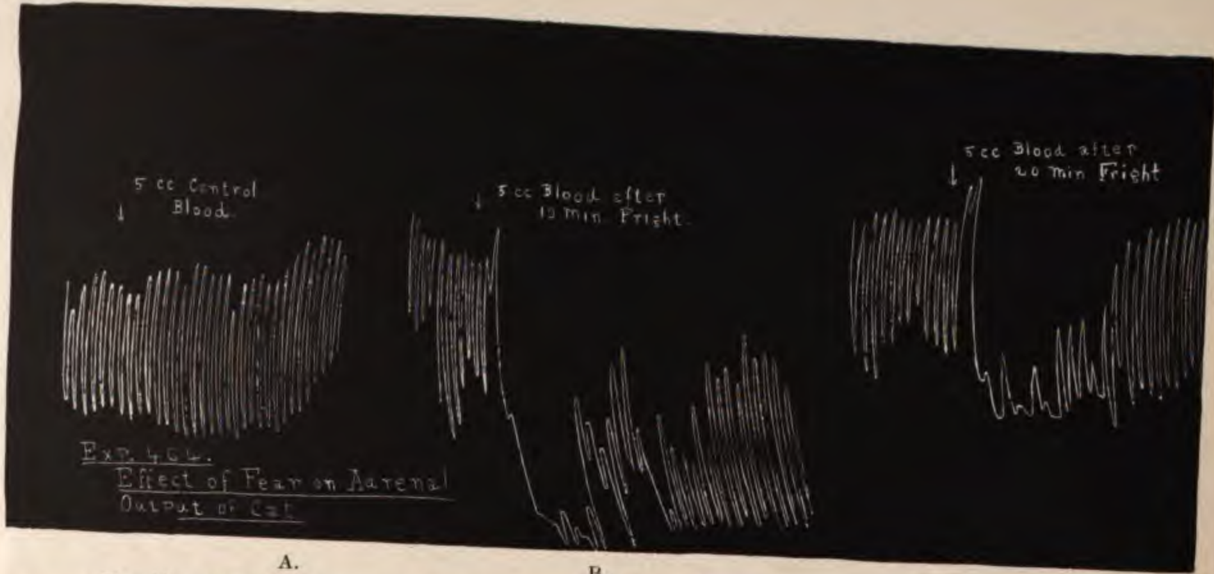
The effect of driving the adrenals is to produce an increased secretion of adrenin, the effect of which in turn is the production of many of the gross phenomena of fear and other emotions, which are also the phenomena of great physical exertion. The effect of adrenin upon the mechanism by which heat and motion are produced in the body is immediate and specific. Adrenin causes an increased output of sugar from the liver — the chief fabricator of the body fuel — and increases the facility with which sugar is consumed in the muscles. When injected into the blood stream, adrenin augments the vigor of the circulation, increases the blood-pressure and the force and frequency of the heart beat and diverts much of the blood supply from the internal organs of digestion and procreation to the skeletal muscles, the lungs and, perhaps, the central nervous system (Cannon).

Simultaneously with the stimulation of organs and tissues necessary to motor activity and the inhibition of organs non-essential to motor activity, adrenin causes erection of the hair, dilation of the pupils, widening of the nostrils, increased activity of the sweat glands, acceleration in the rate and alteration in the rhythm of respiration, rise in body temperature, pallor, trembling, dry mouth, muscular relaxation — many of the phenomena, in short, of fear and rage; phenomena which are also a part of the preparation for an act of supreme muscular exertion. According to Elliot, adrenin performs every function of which the

autonomic nervous system is capable, except that of increasing the output of adrenin.

That this physiologic response to injections of adrenin is equivalent to the act of self-preservation by running or fighting is made obvious by a detailed examination of the significance of each phenomenon. The stimulated organs and tissues are just the organs and tissues that would be most utilized in a struggle for self-preservation by motor activity. The heightened activity of the brain and special senses facilitates the speedier perception of danger and preparation for it. The dilated pupil gives a larger range of vision ; the expanded nostrils a freer intake of oxygen and faster elimination of carbon dioxid to facilitate the increased transformation of energy and neutralization of acid by-products. The activity of the sweat glands tends to regulate the rising temperature. The increased activity of the circulation provides the tissues more readily with fuel and removes more rapidly the accumulation of the waste products of activity. Finally, the energized skeletal muscles consummate the whole adaptive reaction of flight or attack, since it is through these muscles that the teeth, the claws, and the limbs of the moving organism are rendered effective in any form of physical exertion.

On the other hand, the inhibited organs and tissues — the organs of digestion and procreation — are those which would be of no assistance in a time of active struggle. They are the *non-combatants*, so to speak, as the other organs are the active artillery of the body nation at war with environment. The digestive organs are the kitchen and commissary department, the in-



A. B. C.

FIG. 20. — TRACING SHOWING EFFECT OF FEAR ON THE ADRENAL OUTPUT OF A CAT. (Cannon Test.)

The first tracing, A, was made by the contractions of intestinal muscle in blood from a normal cat. The contractions of the intestinal muscle were inhibited when the normal blood was replaced by blood from the same animal after it had been frightened. This inhibition is evidence of increased adrenin in the blood stream, more adrenin apparently is produced in the early stages of fright, B, than in the later stages, C.

dustrial workers and homekeepers, which are necessary adjuncts in time of peace, but excess baggage in time of trouble, and hence, at such a time, are deprived of their energy, for the sake of contributing extra efficiency to the fighting apparatus.

Our experiments show that when normal rabbits are subjected to intense fear from the threatened attack of a dog, the dog being muzzled and not allowed to attack or to chase them, the blood in the *vena cava* of each rabbit, taken from just above the entrance into it of the adrenal vein will show an increased adrenin content.

These observations are in accordance with the findings of Cannon and others, who have shown that adrenin is increased, and the sugar output from the liver correspondingly augmented by rage and fear in cats. (Fig. 20.) On the other hand, no increase of adrenin was found by us in cats which were frightened three months after the splanchnic nerves to the adrenals had been divided.

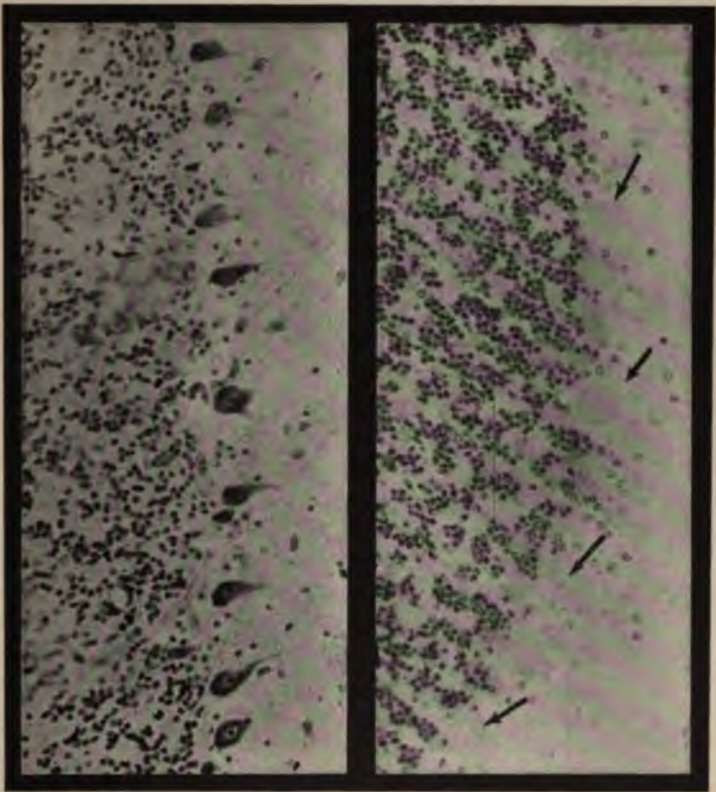
There is abundant clinical evidence to supplement and confirm this laboratory evidence of the connection between the adrenals and distance ceptor stimulation. This evidence is based upon the fact that adrenin causes an increase in the sugar content of both the blood and the urine. Clinicians have long known that emotional excitation causes glycosuria. In cases of *diabetes*, the sugar content is increased in the urine by emotion. Sugar is frequently found in the urine of patients undergoing psychic stress, the glycosuria disappearing after repose. This is in striking contrast to the fact that sugar is rarely found in the urine of

patients or animals which have undergone extensive operations under inhalation anesthesia.

A comparison of the effects of adrenin with those of iodized protein or iodin makes clear at once which is the primary and which the secondary glandular reaction. Adrenin, if exposed to the air, is oxidized in a few minutes; in the blood it is oxidized as quickly. Adrenin acts almost instantaneously, and its effects disappear almost as quickly. On the other hand iodized protein and iodin act more slowly. The effects of a single dose of iodin are not seen for a number of hours — but continue for a day or more even — as do emotions. There is no evidence that adrenin is stored in bulk in the adrenals as iodin is stored in the thyroid, but there is evidence that adrenin is fabricated as needed. It requires more time to fabricate thyreo-iodin. There is evidence, however, that with the ebb and flow of emotion there is an ebb and flow in the store of iodin in the thyroid. These facts make it appear that the secretion of the thyroid determines the key in which adrenin plays the tune of life.

Relation of the Liver to Distance Ceptor Stimulation

In addition to the experimental and clinical evidence that chemical or histologic changes are produced by emotion in the brain, thyroid and adrenals, we have evidence that as a result of the transformation of energy in emotion, histologic changes are produced in the liver also. As a result of any increased energy transformation in the body there is an increased formation of acid by-products, with a rresponding increase in the activity of the mechanism



A. Section of normal cerebellum of rabbit.

B. Section of cerebellum of rabbit showing effect of extreme emotion (fright).

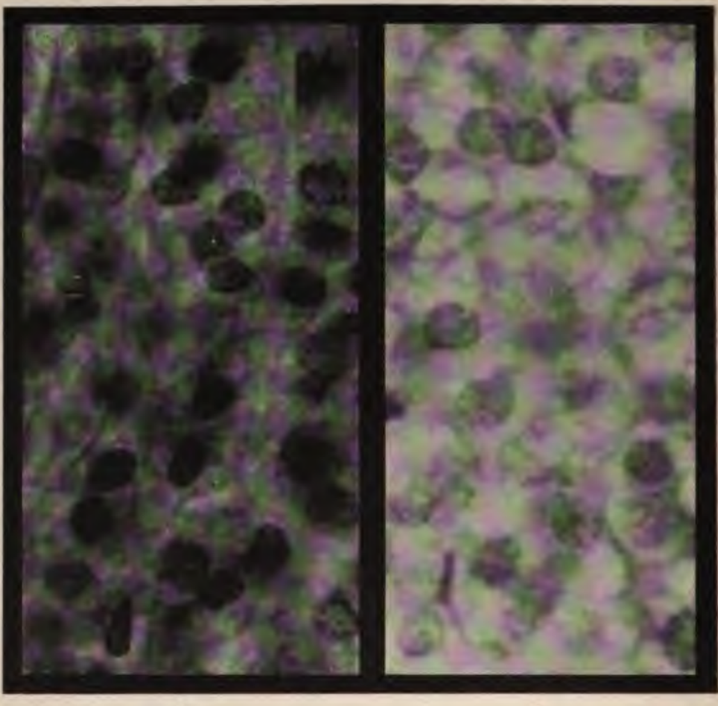
Fig. 21. — Photomicrographs Showing Effect of Fright on the Brain-cells of a Rabbit.

Note the almost complete disappearance of Purkinje cells in B. (See arrows.)

(From photomicrographs, × 310.)

for the neutralization of acids, a primary factor of which is the liver. These observations but confirm common experience and the specialized knowledge of

the medical observer regarding the intricate relation existing between the function of the liver and the emotions.



A.
Section of normal adrenal of rabbit.

B.
Section of adrenal of rabbit showing effect of extreme emotion (fright).

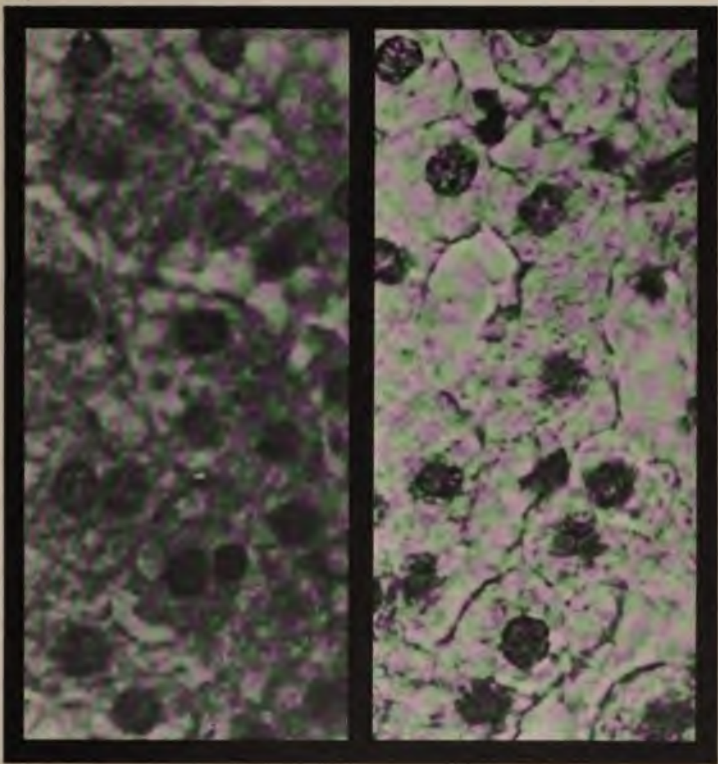
FIG. 22. — PHOTOMICROGRAPHS SHOWING EFFECT OF FRIGHT ON THE ADRENALS OF A RABBIT.

In B note the widespread loss of cytoplasm and the disappearance of nuclei.

(From photomicrographs, × 1640.)

The evidence that functional and histologic changes are produced in the brain, thyroid, adrenals and liver by the emotions, together with the outward manifes-

tations of emotion, gives convincing proof that the response to distance ceptor stimulation is as auto-



A. Section of normal liver of rabbit.

B. Section of liver of rabbit showing effect of extreme emotion (fright).

Fig. 23. — Photomicrographs Showing the Effect of Fright on the Liver of a Rabbit.

(From photomicrographs, × 1640.)

matic and specific as are the responses to contact or chemical ceptor stimulation. (Figs. 21, 22, 23.)

Explanation of the Gross Phenomena of the Emotions

In the light of this evidence many phenomena of fear and of other emotions may be explained. It is known, for instance, that men and animals under the stimulus of strong emotion possess an extraordinary amount of physical strength. This is explained by the fact that fear drives certain organs and inhibits others so that every particle of available energy is concentrated upon the fighting mechanism. The advantage that this power must have given to prehistoric man in his struggles against superior foes in a wild environment is apparent to any one who will allow his imagination to revert to those days of supreme physical contest. But that the tendency should persist to-day, in spite of the disappearance of most of the stimuli to active physical combat, so that, at the slightest hint of danger, man's energies are drained, exactly as in the days of physical struggle, is one of the misfortunes of our insufficiently adapted state.

So strong is the force of these ancestral acts, so firmly established the action pattern of muscular response to the fear stimulus, that now, whether a business catastrophe or an attacking enemy threaten, fear is expressed in terms of the ancestral flight to safety or fight for life which took place in the remote brute period of human history. In spite of the fact that by harnessing the forces of nature, and by social coördination, which reduces the number of motor reactions, man has progressed vastly in his methods of acquiring food and avoiding danger, his body still responds to threatened moral or financial disaster, as if the old

need for physical contest remained. His heart beats wildly; his respirations are quickened; he trembles and turns cold; his knees shake; beads of sweat stand upon his brow; he is pale and his mouth is dry; he feels faint and may collapse. Whether the cause of fear be moral, social, financial or intellectual, the result is the same. There is not one form of fear for the defaulting bank president and another for a hunter facing his first game; not one group of fear phenomena for a mother anxious for her sick child, another for a friend waiting for news from the battlefield, and still another for the soldier facing a superior foe. In every case it is the same fear — fear of bodily harm — expressed in terms of bodily activation, and involving every organ and tissue, which would be involved were the natural phylogenetic response of flight from an enemy consummated in muscular exertion.

Although there is no absolute proof, yet there is much evidence to show that the effect of emotion without action is injurious, apart from the actual exhaustion of potential energy and the increased acid by-products. It is well known that the soldier lying under fire awaiting orders to advance suffers more keenly than the soldier who flings himself actively into the fray. The wild animal in captivity suffers more than the same animal in the struggle for existence in its native woods or plains. Many wild animals in captivity refuse food, sleep little, emaciate rapidly and die. An individual nursing a grievance in secret is measurably improved in health and disposition by giving vent to his anger in physical combat. The presence in the body of various energizing secre-

tions, such as the secretions of the thyroid and the adrenals, needed for physical combat, but not used in emotion, apparently is injurious.

As fear activates the body, so all emotions and psychic states activate the body and exhaust energy in proportion to the degree in which they represent the physical activity attendant upon the phylogenetic forms of self-defense. As fear recapitulates the ancestral act of flight from an enemy, so rage or anger recapitulates the act of attack and in like manner activates the muscles that would be used were the physical fight made.

On the same hypothesis love becomes the representation of ancestral conjugation — the activation of the entire motor mechanism for copulation without action. The phenomena attendant upon the emotion — the quickened pulse, the leaping heart, the accelerated respiration, the sighing, the glowing eye, the crimson cheek — are all eloquent testimony to the activation which may become a definite cause of serious physical breakdown. In certain circumstances it is difficult for even the experienced physician to determine whether a patient exhibiting emaciation, indigestion, insomnia, nervousness and cardiac irritability is suffering from continuous worry during a prolonged and intense struggle for existence or from unrequited love. The profound transformation wrought in the entire personality by the removal of the stimulus of worry is equivalent to that wrought by the consummation of love in marriage.

As fear, anger and love express the motor acts of flight, attack and conjugation, so the emotions of

anxiety, anticipation, disappointment, grief, despair, envy, jealousy may all be regarded as lesser or chronic forms of these major activations. Grief is defeat, the epitome of desperate but unsuccessful struggle. Envy is a chronic form of rage, adding each day a little to the burden of waste matter, which is doubtless sufficient to account for the "bilious" aspect which is ascribed to the envious. In like manner the more abstract concepts involved in the intellectual processes of logic, invention, mathematics and artistic fancy may be explained as representations of the primary activities involved in the creation of the arts and the sciences. Addition was once the placing of one stone upon another.

Summary and Conclusion

In this and the foregoing chapters, we have treated the reactions of the organism from the usual *biologic viewpoint* only as manifestations of the adaptation of the organism to its external and its internal environments. We have attempted to show that the reactions of the organism are specific to the exciting stimuli and appear in an order of sequence, which may be compared to the response of an electric motor driven by a battery. Pressing the button is the adequate stimulus which travels to the motor causing the transformation of stored energy into heat and motion. If the motor and battery are driven long enough, exhaustion and physical changes are produced.

It is necessary to realize that every reaction, by which life is manifested in the organism and adaptation to environment secured is the result of the trans-

formation of energy in the organism. The human organism, like plants and other organisms, is fundamentally a transformer of energy, this energy being derived originally from the external environment and returned ultimately to the environment, in the form of heat, motion, electrical energy, mechanical work performed, etc.

In the present chapter we have considered in part the action of this effector mechanism, in showing the participation of certain organs in the production of the reaction which we term *emotion*. In the succeeding chapter, we propose to show that a system of organs has been evolved for the specific purpose of transforming potential into kinetic energy for the principal reactions in the body. This system of organs we propose to call the *Kinetic System*. A consideration of the reason for the evolution of such a mechanism; proof that it does perform the function predicated for it; and indications of the important bearing, which a knowledge of this function may have upon an interpretation of medical problems, as well as of the phenomena of normal life, are contained in the following chapters.

CHAPTER VI

THE KINETIC SYSTEM

Function of a Kinetic System

THE adaptation of man and kindred animals to environment is secured by a series of physical and chemical reactions which are the outward expressions of a transformation of energy, by which the forces latent in food products that have been appropriated and stored in the organism are released to produce heat and motion. In this transformation of energy certain organs perform such prominent rôles, and perform them so uniformly, that we conclude that these organs coöperate as a system whose specific function is to transform potential into kinetic energy for adaptive reactions.

Let us first see how the postulation of such a system in the human organism would affect the rôles of other recognized systems in the body, and the parts they play in the conversion of energy. Man appropriates from his environment the energy he requires in the form of crude food, which is refined by the *digestive system.* Oxygen is taken to the blood and carbon dioxid is taken from the blood by the *respiratory system.* To and from the myriads of working cells of the body, food, oxygen and waste are carried by the *circulatory system.* The body is cleared of waste by the *urinary system.* Procreation is accomplished by the *genital system.* Each

of these systems in performing its specific functions transforms a certain amount of potential into kinetic energy for the accomplishment of its specific purpose, but not one of them transforms latent into kinetic energy for the purpose of escaping, fighting, pursuing or combating infection, which are essentially adaptive reactions. Obviously, therefore, none of these systems transforms potential into kinetic energy *primarily* for these adaptive reactions. The stomach, the kidneys, the lungs, the heart, strike no physical blow; their rôle is to do certain work, to transform energy that the blow may be struck by another system, which we believe has been evolved primarily for that purpose. In the present chapter we shall offer evidence that there is in the body a system of organs, which we shall term the *Kinetic System,* which is specifically adapted to transform potential into kinetic energy for the production of heat and motion. The principal organs comprising the kinetic system are the brain, the thyroid, the adrenals, the liver and the muscles. The brain is the great central battery which drives the body; the thyroid governs the conditions favoring tissue oxidation; the adrenals govern immediate oxidation processes; the liver fabricates and stores glycogen, and is the great neutralizer of the acid products of energy transformation; and the muscles are the final converters of latent energy into motion and heat. While the kinetic system does not directly circulate the blood, exchange oxygen and carbon dioxid, perform the functions of digestion, urinary elimination or procreation, it does play an important rôle in each of these processes. In turn, digestion, elimination, procreation,

etc., may be regarded as aiding materially, though indirectly, in the function of the kinetic system.

Adaptive Variation in Amount of Energy Stored in Different Animals

In considering the evolution of such a system in the human organism two points demand special attention: the *amount* of potential, transformable energy which is stored in the animal body in excess of the needs of the moment; and the *variation* in rates of speed at which this store must be expended in accordance with the dictates of any specific adaptive reaction. In general, the amount of available, *convertible* energy resident in living organisms appears to be proportional to the dependence of the organism upon motor activity for survival. That is, as we ascend the life scale from the stationary species and animals protected by such mechanical contrivances as shells and barbs, poisons, odors and emanations, and approach animals which depend entirely upon power and speed for survival, we find an increasing need for the storage of energy in great excess of the needs of the moment and for discharging that energy and overcoming the consequent acid by-products at varying rates.

It is conceivable that plants and polyps, which make little change in their position throughout life, have no need for an elaborate kinetic system. The snail, the turtle and crustacea generally, protected by their shells, are proverbially slow of motion, and it is difficult to exhaust the small supply of convertible energy which is all that is required for their sluggish routine reactions. The horse and the deer, on the other hand,

the easily excited antelope, the spider monkey and certain dynamic inhabitants of the sea, such as the trout and the salmon, apparently hoard a supply of convertible energy far in excess of the routine needs of feeding and multiplying.

As for man, who is just emerging from an environment in which muscular efficiency has been of paramount importance to survival, in fighting and searching for food, in fleeing from enemies, in building safe havens, in pursuing and winning mates, and in accomplishing procreation, the need for variation in dynamic expenditure is obvious.

Variation in Rate of Energy Transformation in the Individual

The rate of energy transformation varies not only in different species of the animal kingdom, but in individuals of the same species, and in different periods of the life of the individual. Thus, peoples who have lived long in an environment of natural plenty, who have had to exert themselves but little to make a living, show few and simple reactions as compared with the more strenuous members of continually warring communities. To compare the natives of our tropical plantations, or of the fertile valley of the Nile, with the dynamic-tempered Jew and other urban-born and business-disciplined inhabitants of seething cities is like comparing the turtle with the spider monkey.

In the life cycle of the individual organism there are ı long and short periods of increased activity to h the organism must become adjusted. The out- of energy must meet the varying requirements of

different seasons of the year, of the long cycles of growth, reproduction and decay, of the unbalanced demands of consciousness and of sleep, of health and of disease, of activity and of rest.

One of the most conspicuous periods of increased activity is the breeding season of most animals, which occurs in advance of the period of maximum food supply, that the young may be brought forth at a time when food is plentiful. In the spring most birds and mammals mate, to the accompaniment of the increased activities which are expressed in song and courting, in fighting and flying, in quickening pulse and increased temperature. In the spring the chief activating gland of the kinetic system, the thyroid, shows a distinct enlargement. Even more activation than is represented by the seasonal activities is represented by the physical act of mating, when the thyroid is known to enlarge, and life is on a sensuous edge.

In like manner the expenditure of energy in the organism varies for the day and the night; for youth and age. The full tide of activity and consciousness is in the daytime; the ebb tide at night. The youth is geared at high speed for growth, for becoming adapted to innumerable injuries, to bacterial invasions, to heterogeneous food and to the various elements in his external environment.

The period of greatest energy output for physiologic ends is the period of reproduction. In the female especially there is a period of greatly increased activity just prior to her development into the procreative age. During this time secondary sexual characters are being developed. The pelvis expands; the ovaries and

the uterus grow rapidly; the mammary glands develop. At this period of increased expenditure of energy for physiological adjustment, there is a correspondingly rapid growth in the thyroid, the adrenals and the hypophysis. Without the normal development of the adrenals, the thyroid and the hypophysis, neither the male nor the female can develop secondary sexual characteristics, show sexual desire, seasonal cycles of activity or power to procreate. On the other hand, all these phenomena — secondary sexual characters, sexual desire, fertility — can be created in the organism by feeding the thyroid products of an alien species to the individual deprived of a thyroid.

At the close of the child-bearing period there is a permanent diminution in the rate of energy conversion, consistent with the fact that energy is no longer needed for procreation and that less is required for self-preservation. Unless other factors intervene, this reduction in the rate of energy transformation, together with a corresponding reduction in the size of the thyroid gland, is progressive until senescent death.

The Purpose and the Mechanism of Heat Production

As the organism transforms potential into kinetic energy for the production of these various types of visible and invisible motion, so it transforms energy for the adaptive reaction of *heat*.[1] A by-production of heat always accompanies every production of muscular activity in the human body, but that this is not a useful adaptation may be inferred from the fact that a

[1] The terms "heat" and "muscular action" are not used here in a purely physical sense, but to designate physiological phenomena.

mechanism for heat elimination (sweating) is stimulated simultaneously with the initiation of muscular or emotional activation. Heat as a by-product of muscular action, therefore, does not concern us, but rather heat as an adaptive defense against foreign proteins and infection. Vaughn has shown that the presence in the body of any alien protein causes an increased production of heat, and that there is no difference between the production of fever by foreign proteins and by infection. Before the day of the hypodermic needle and of experimental medicine, the foreign proteins found in the body outside of the alimentary tract were brought in by invading microörganisms. Such organisms interfered with life and often destroyed the host. To attain survival, therefore, the body was forced to evolve a defense against these menaces.

That the production of fever is a protective adaptive response is rendered probable by the following facts: First, and of minor importance, bacteriologists have shown that pathogenic bacteria grow best at the normal temperature of the human body, and that any increase in temperature has a tendency to hinder the growth and in some instances to kill the invading organisms. Second, either living or dead foreign proteins may be split up and cast off, just as excessive protein food is broken down and cast off from the body. The organism is protected against self-destruction in this splitting-up process by its specific adaptation for withstanding the agency (excessive metabolism) which accomplishes this chemical purification. That chemical purification is facilitated by the production of fever is suggested by the fact that with each rise in

temperature of one degree centigrade the metabolic activity in the body is increased ten per cent. This increase in the expenditure of energy is not compensated by an increased intake of food, since in acute infection there is aversion to food and often vomiting. In infection, as in fear, therefore, it would seem as if the combined resources of the body were concentrated upon the effort at chemical self-defense; and in the furious combustion to attain this end the host himself is often destroyed.

We assume that the mechanism which transforms potential energy into kinetic energy to produce muscular action is the brain-muscular apparatus, assisted by the activating and accelerating organs, the thyroid and the adrenals. We postulate that the mechanism which produces muscular action and emotion is the same as the mechanism which generates heat, maintains consciousness, and causes the splitting up of foreign proteins by which the chemical purity of the body is maintained. Unless this be true, our argument for a kinetic system fails.

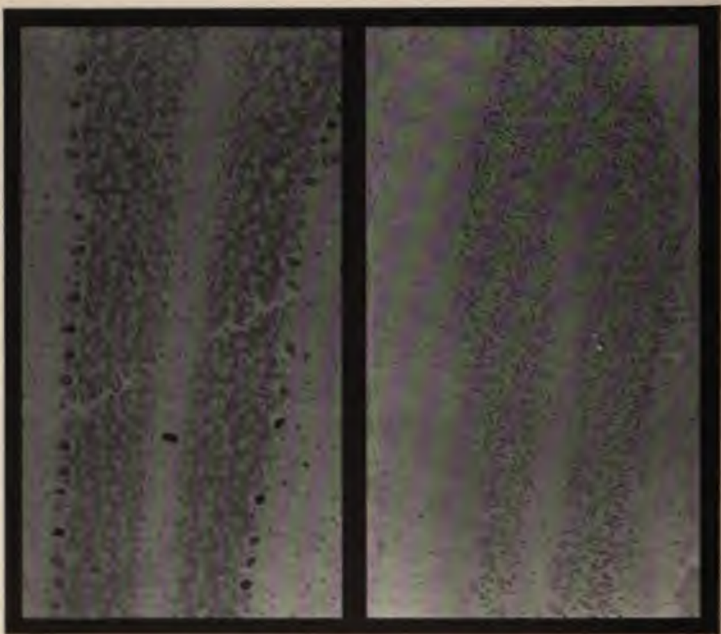
Histologic Changes in the Brain, the Liver and the Adrenals in Relation to Transformation of Energy

If the brain, the thyroid, the adrenals, the liver and the muscles work together in transforming potential into kinetic energy for the adaptive reactions of heat and motion, we should find similar changes in these organs whatever may be the purpose of the conversion of energy — whether for the production of motion in running or fighting or for the production of heat in combating infection. We should find also that these

changes are the result of the activating stimuli causing the reactions, or of the effort to reëstablish the normal standard of chemical purity after the reactions; and that the generation of heat and motion does not produce equivalent changes in other organs and tissues of the body. If our premise be sound, these changes in the organs of the kinetic system would accompany the transformation of energy necessary for the routine conduct of the body, as well as for the additional drafts of energy required for "emergency" reactions. That is, the transformation of energy is necessary for the mere maintenance of consciousness and a normal body temperature, as well as for the production of motor activity in physical exertion, in fighting and in combating infection.

To test these points we planned an experiment whose purpose was to apprehend as in a net the active participants in the process of energy transformation as far as histologic changes could show them. Groups of rabbits were kept awake continuously from 90 to 112 hours by relays of students. They were given abundant food and water and were subjected to no physical violence, fear, drugs or infection. Their external and their internal environments were normal excepting that they were not allowed to sleep. At the end of the periods of insomnia all the animals were exhausted, some to the point of death. All were killed, some immediately, others after varying periods of rest; and *every organ and tissue in the body was examined for histologic changes.* In some cases observations of the H-ion concentration of the blood were made. Some animals were given nitrous oxid anesthesia as a substitute for sleep. To

determine whether or not the lesions in the brain, the adrenals and the liver caused by exhaustion could be repaired by rest without sleep, other animals were first fatigued by physical exertion and then kept awake



A. Section of normal cerebellum of rabbit.

B. Section of cerebellum of rabbit after insomnia — 100 hours.

FIG. 24. — PHOTOMICROGRAPHS SHOWING THE EFFECT OF INSOMNIA — 100 HOURS — ON THE BRAIN-CELLS OF A RABBIT.

Compare the well-stained clearly defined Purkinje cells along the margins of section A with the faint traces of the Purkinje cells which are barely visible along the margins of section B.

(From photomicrographs, × 100.)

for eight hours, their tissues being compared with those of similarly fatigued animals which were allowed immediate sleep. In every case we made histologic examina-

A. Section of normal adrenal of rabbit.

B. Section of adrenal of rabbit after insomnia — 100 hours.

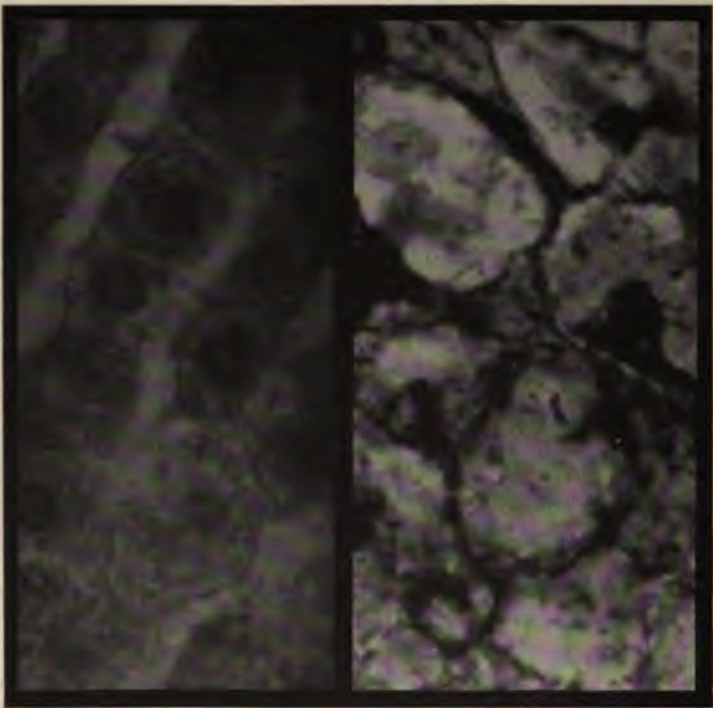
FIG. 25. — PHOTOMICROGRAPHS SHOWING THE EFFECT OF INSOMNIA — 100 HOURS — ON THE ADRENALS OF A RABBIT.

Compare A and B, noting in the latter the disappearance of cytoplasm, the loss of some nuclei and the generally disorganized appearance of the cells.

(From photomicrographs, × 1640.)

tions of the brain, the hypophysis, the salivary glands, the thyroid, the parathyroids, the thymus, the lymphatic glands, the lungs, the heart, the liver, the pancreas, the stomach, the intestines, the spleen, the

adrenals, the sex organs, the kidneys, the bone marrow, the blood and the muscles. As compared with the corresponding tissues of normal animals, all these organs



A. Section of normal liver of rabbit. B. Section of liver of rabbit after insomnia — 100 hours.

FIG. 26. — PHOTOMICROGRAPHS SHOWING THE EFFECT OF INSOMNIA — 100 HOURS — ON THE LIVER OF A RABBIT.

Compare A and B, noting the vacuolated spaces and general loss of cytoplasm in the latter.

(From photomicrographs, × 1640.)

d tissues were normal with three exceptions. The ain, the adrenals and the liver alone showed arked and widespread histologic changes as a result

of the prolonged consciousness. (Figs. 24, 25, 26.) In the animals which were allowed eight hours of sleep at the close of the period of insomnia these organs were

A. Section of normal cerebellum of cat. B. Section of cerebellum of cat showing effect of extreme physical exertion.

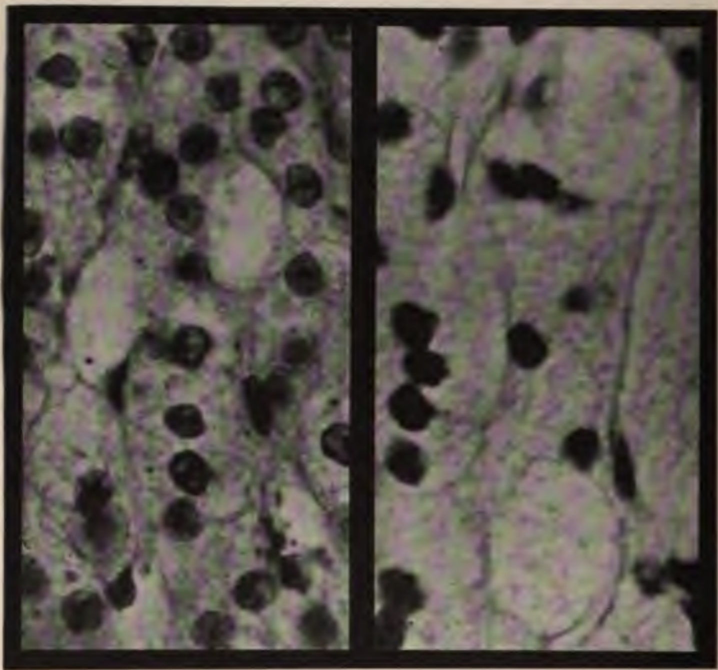
FIG. 27. — PHOTOMICROGRAPHS SHOWING THE EFFECT OF EXERTION ON THE BRAIN-CELLS OF A CAT.

Note the general disintegration of the Purkinje cells in B.

(From photomicrographs, × 310.)

restored to their normal histologic condition with the exception of some cells in the brain and the liver which had been irreparably damaged.

Another group of animals, kept awake for from 90 to 112 hours, instead of being allowed to sleep naturally, were placed for eight hours under nitrous oxid anesthe-



A. Section of normal adrenal of cat.

B. Section of adrenal of cat showing effect of extreme physical exertion.

FIG. 28. — PHOTOMICROGRAPHS SHOWING THE EFFECT OF EXERTION ON THE ADRENALS OF A CAT.

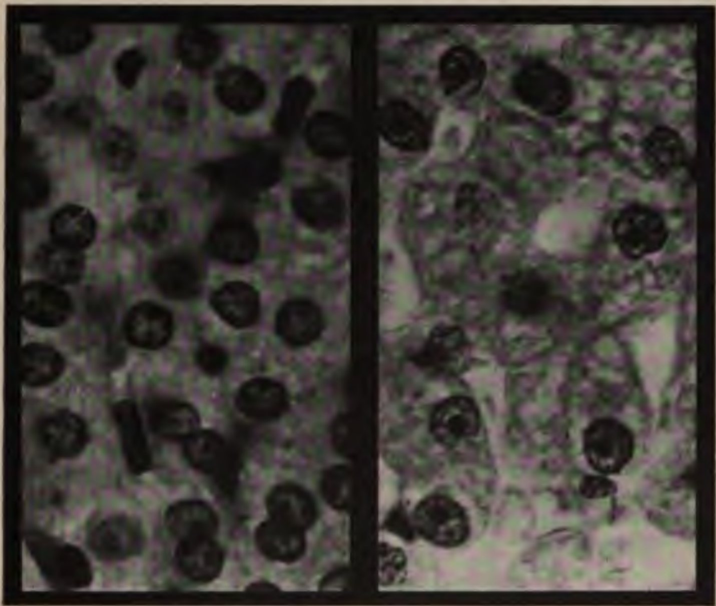
In B, note the general loss of cytoplasm and the disappearance of many nuclei.

(From photomicrographs, × 1640.)

sia. Of the brain cells of these animals ninety per cent were found to be hyperchromatic, resembling closely the abnormally large percentage of hyperchromatic

cells in the brains of hibernating woodchucks; but the percentage of exhausted cells was increased also.

Having noted the effect of exhaustion by insomnia upon the brain, the adrenals and the liver, we repeated the investigation in other typical cases of exhaustion



A. Section of normal liver of cat.

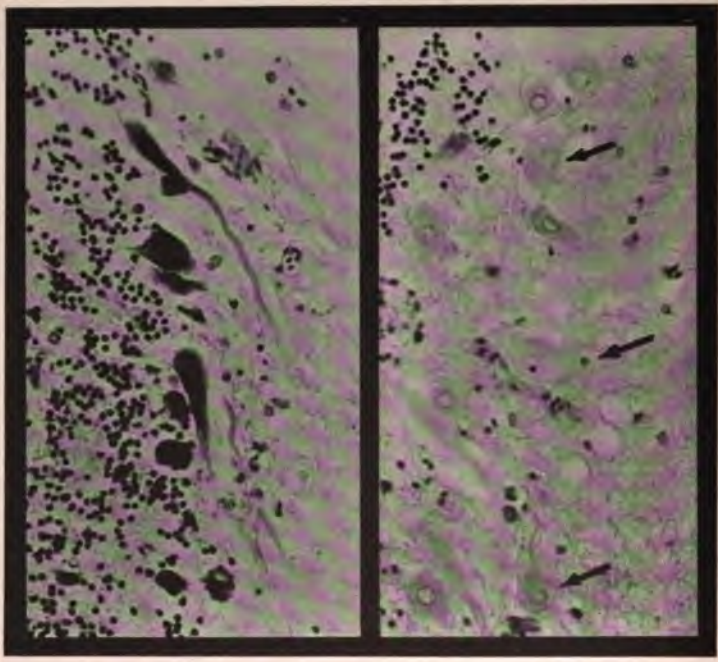
B. Section of liver of cat showing effect of extreme physical exertion.

Fig. 29. — Photomicrographs Showing the Effect of Exertion on the Liver of a Cat.

In B, note the vacuolated spaces and the disappearance of many nuclei. (From photomicrographs, × 1640.)

by physical and chemical stimuli. We examined the organs of animals exhausted by the muscular work of running and fighting (Figs. 27, 28, 29); the organs of foxes chased by hounds; of dogs and woodchucks ex-

hausted by fighting; of electric fish before and after electric discharge; of salmon before and after their exhausting run up the Columbia River to their spawning beds. (Figs. 30, 31, 32.) We examined the organs



A. Cerebellum of salmon from ocean. B. Cerebellum of salmon from headwaters of Columbia River.

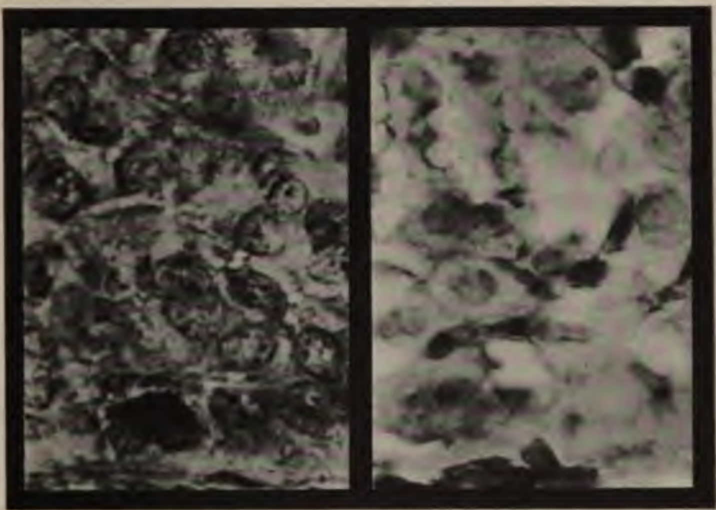
FIG. 30. — EFFECT OF A LONG SWIM ON BRAIN-CELLS OF A SALMON.

Exhaustion is shown by the disappearance of chromatic material from the Purkinje cells in B.

(From photomicrographs, × 310.)

of animals exhausted by excessive emotional excitation; of animals exhausted by strychnin convulsions; of animals to which had been given alcohol, nicotin, morphia, scopolomin, ether and nitrous oxid; of animals

subjected to injections of colon, tetanus, diphtheria and typhoid bacilli and to the toxins of gonococci, streptococci and staphylococci; of animals activated by injections of indol, skatol, leucin and creatin (Figs. 33, 34, 35); the organs of human beings who had died of long and wasting diseases, such as typhoid fever,



A.
Section of adrenal of salmon from ocean.

B.
Section of adrenal of salmon from headwaters of Columbia River.

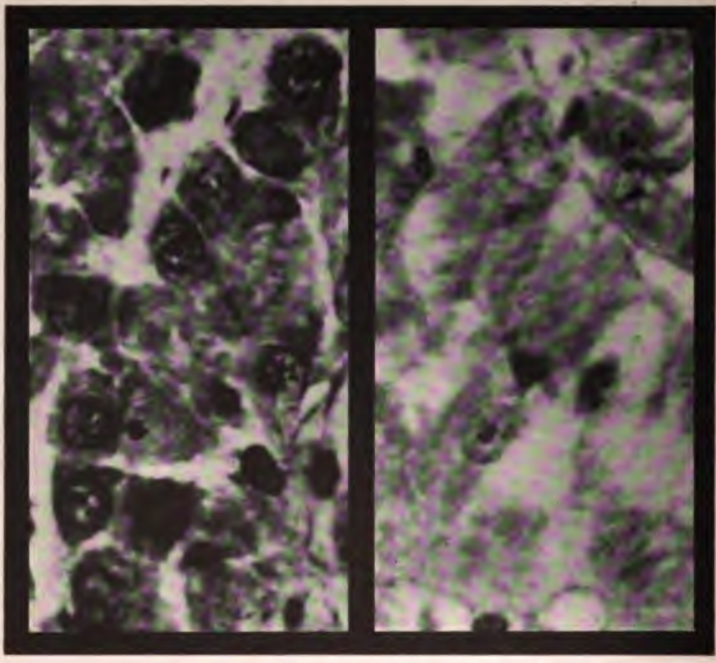
FIG. 31. — EFFECT OF A LONG SWIM ON THE ADRENALS OF A SALMON.

Note the disappearance of cytoplasm and the generally disorganized appearance of the cells in B.

(From photomicrographs, × 1640.)

Graves' disease, cancer, tuberculosis, pyogenic infections, tetanus, chorea, toxemia from intestinal obstruction, toxemia from gangrenous intestine, hemorrhage, eclampsia, acute acidosis and uremia. (Figs. 36, 37.) We observed the effects of foreign proteins, of pep-

tones, of iodin, of thyroid extract, of adrenalin, of acids and alkalis. We examined the organs and tissues of animals from which the adrenals, the pancreas or the liver had been excised; the organs of animals given



A. Liver of salmon from ocean.

B. Liver of salmon from headwaters of Columbia River.

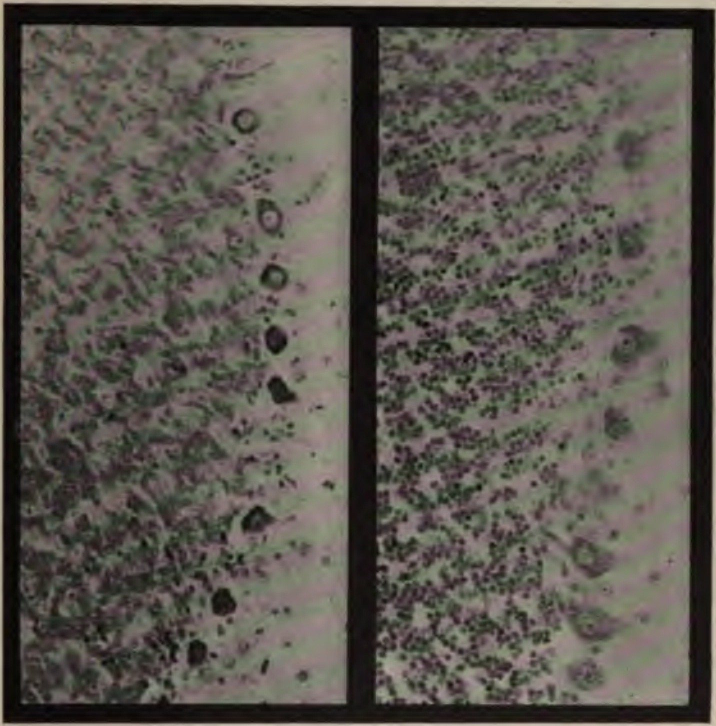
FIG. 32. — EFFECT OF A LONG SWIM ON THE LIVER OF A SALMON.

Note the eccentric position of nuclei, disappearance of cytoplasm, and generally disorganized appearance of cells in B.

(From photomicrographs, × 1640.)

toxins and strychnin while under various forms of anesthesia; of animals given strychnin under anesthesia and while under the influence of curare; of animals

first given heavy doses of opium, then traumatized, or given toxins, acids, strychnin and adrenin.



A. Section of normal cerebellum of cat.

B. Section of cerebellum of cat after injections of indol and skatol.

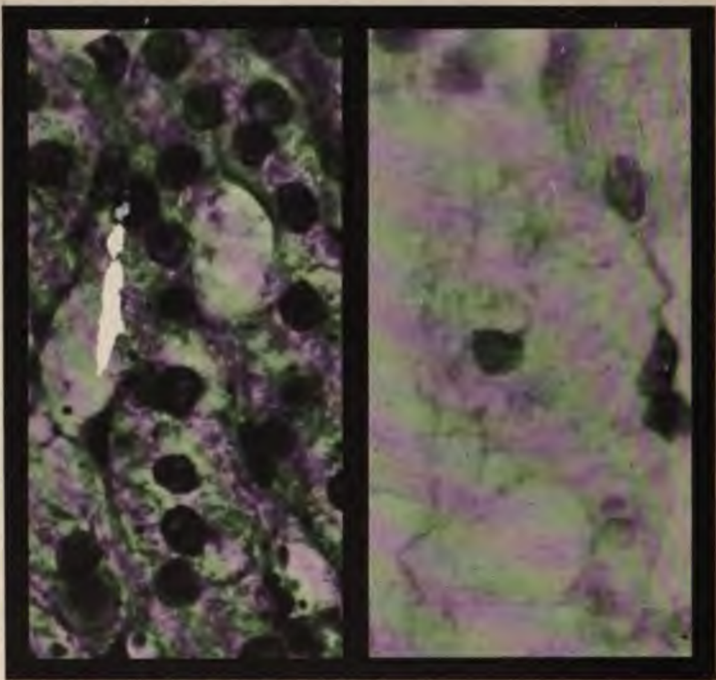
FIG. 33. — EFFECT OF INJECTIONS OF INDOL AND SKATOL ON THE BRAIN-CELLS OF A CAT.

Compare the Purkinje cells in B with those in A, noting the hypochromatism and the general appearance of disorganization in B.

(From photomicrographs, × 310.)

As a contrast to these studies histologic examinations were made of normal animals; of animals after long sleep — woodchucks immediately after hibernation.

These studies, which have extended over a period of six years, and have included the classification of over one hundred thousand brain cells, show that in every



A. Section of normal adrenal of cat.

B. Section of adrenal of cat after injections of indol and skatol.

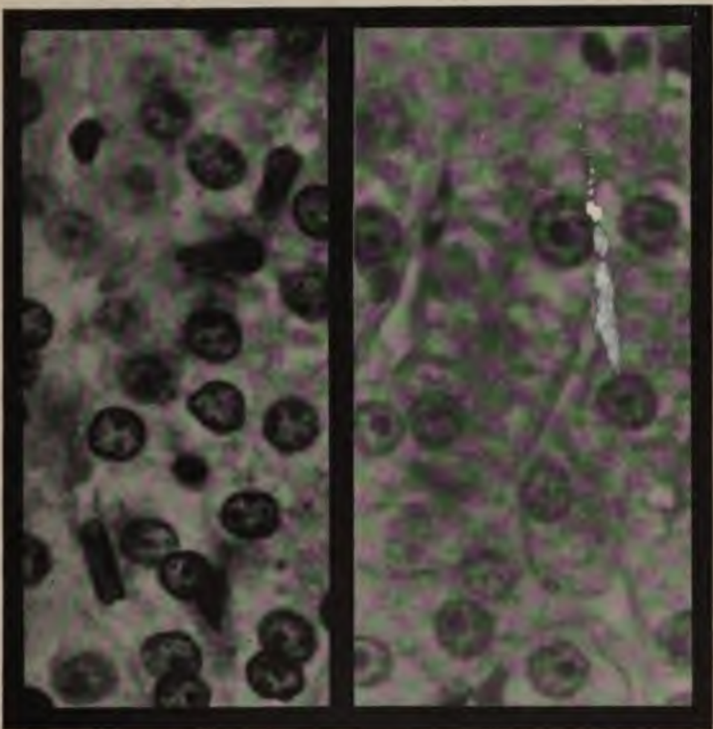
Fig. 34. — Effect of Injections of Indol and Skatol on the Adrenals of a Cat.

Note the widespread disappearance of cytoplasm and of nuclei in B.

(From photomicrographs, × 1640.)

instance of exhaustion, except when the vitality had been depressed by narcotics and anesthetics, identical changes were produced in the *same three organs — the brain, the adrenals and the liver.* Whatever the cause of

exhaustion the amount of cellular deterioration — as nearly as could be estimated — was proportional to the degree of exhaustion and involved all parts of the cer-



A. Section of normal liver of cat.

B. Section of liver of cat after injections of indol and skatol.

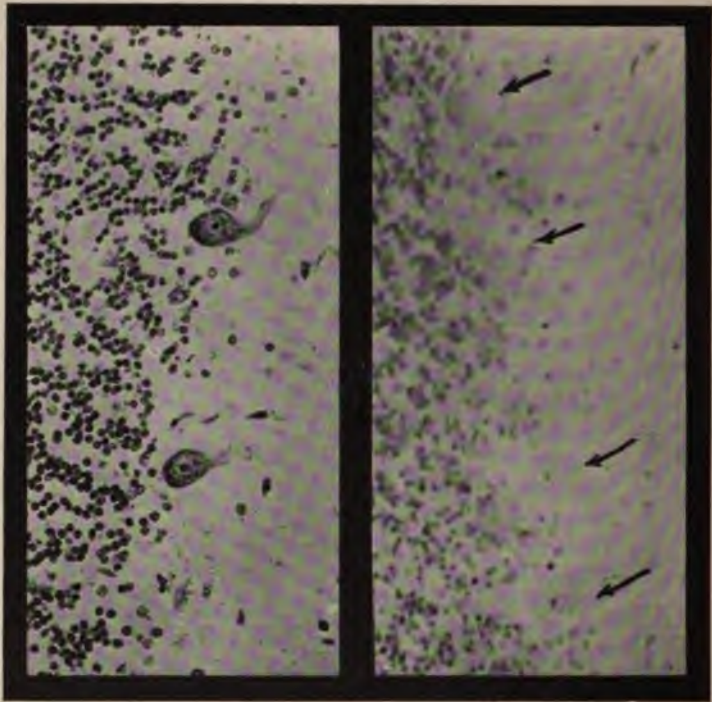
FIG. 35. — EFFECT OF INJECTIONS OF INDOL AND SKATOL ON THE LIVER OF A CAT.

Note the disappearance of cytoplasm and of many nuclei in B.

(From photomicrographs, × 1640.)

ebro-spinal axis, being most noticeable in the higher centers. In exertion, emotion, traumatic shock, infection, foreign protein reaction and insomnia, the cycle

N



A. Section of normal human cerebellum (after accidental death).

B. Section of human cerebellum after death from carcinoma.

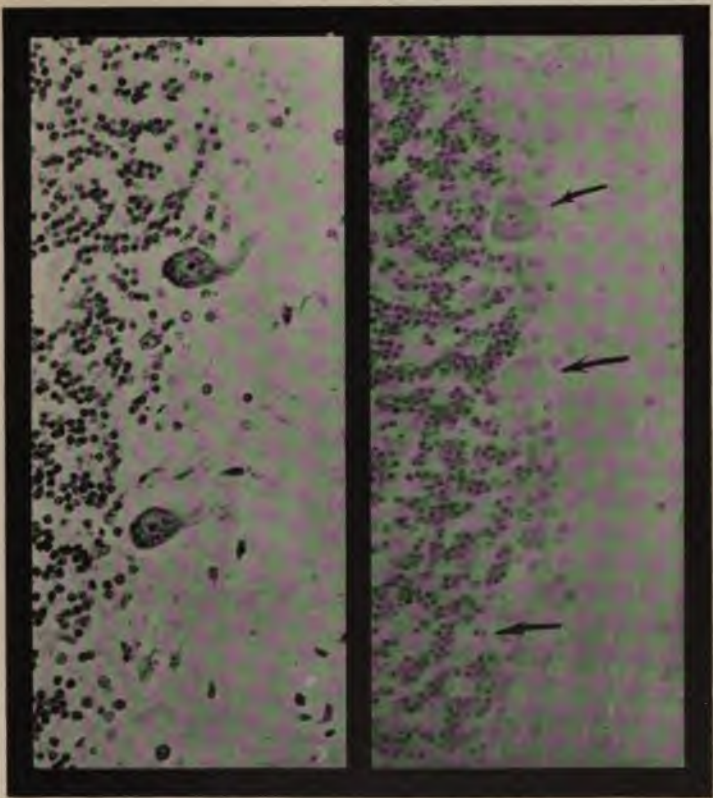
FIG. 36. — EFFECT OF CARCINOMA ON THE BRAIN-CELLS OF A HUMAN BEING.

All the Purkinje cells in focus in B show loss of chromatic material. In some (indicated by arrows) the evidence of deterioration is so great as to leave but the faintest outline of the cell.

(From photomicrographs, × 310.)

of change was from a first stage of hyperchromatism to chromatolysis and the physical breakdown of some cells.

Whether the stimulating agent was physical exertion, prolonged emotional excitation, severe injury, the injection of strychnin, the toxins of disease, or the persistent maintenance of consciousness under normal conditions,



A. Section of normal human cerebellum (after accidental death).

B. Section of human cerebellum after death from paratyphoid fever.

FIG. 37. — EFFECT OF PARATYPHOID FEVER ON THE BRAIN-CELLS OF A HUMAN BEING.

In B note the general loss of chromatic material and the almost entire disappearance of some Purkinje cells (indicated by arrows).

(From photomicrographs, × 310.)

mattered not; the functional manifestations and the histologic changes produced in the brain, the adrenals and the liver were identical. It is evident, therefore, that whatever other organs may be involved in the

transformation of energy, the brain, the adrenals and the liver bear their portion of the stress of life — take their portion of the work of producing activity, and also, as we shall see later, the burden of repairing the effects of activity.

Functional Changes in the Adrenals in Relation to Transformation of Energy

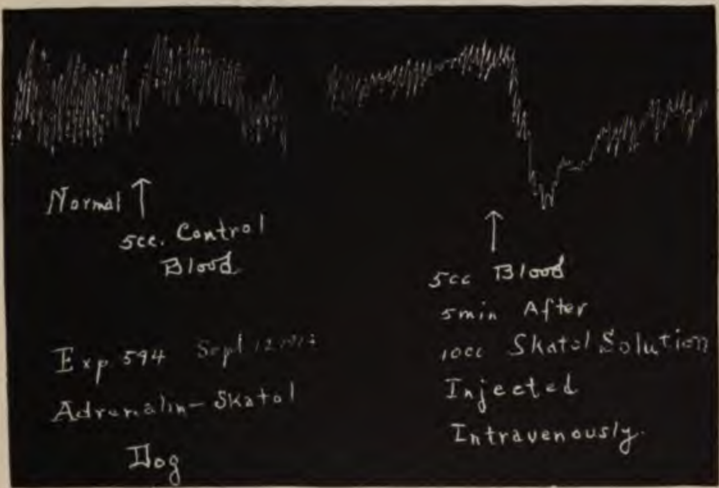
The identical *functional* changes in the adrenals under activation are as significant as are the identical histologic changes in the brain, the adrenals and the liver. In our experiments the types of activation that produced histologic changes in the brain, the adrenals and the liver produced an increased output of adrenin. The functional activity of the adrenals was determined (1) by the biologic test [1] and (2) by the determination of the H-ion concentration of the blood in the adrenal veins before and after activation.

In examinations of the blood of sixty-six animals subjected to rage, fear, anaphylaxis, injections of indol, skatol, leucin, creatin, toxins of diphtheria, colon bacilli, foreign proteins and strychnin, *the biologic test for adrenin was positive.* (Figs. 38, 39.) *In brief, the agencies which caused histologic changes in the brain, the liver and the adrenals, with the single exception of traumatism under anesthesia, caused an increased functional activity of the adrenals.*

H-ion concentration tests showed that the blood in the adrenal veins was more alkaline than the blood from the brain, muscles, pancreas, liver, thyroid,

[1] Inhibition of intestinal muscle.

spleen or kidneys. Adrenin itself is more alkaline than normal blood. The H-ion concentration of the blood in the adrenal vein as compared with that of the blood in other parts of the circulation is therefore an index of the amount of adrenin in the blood. We found an increased H-ion concentration in intense emotion;



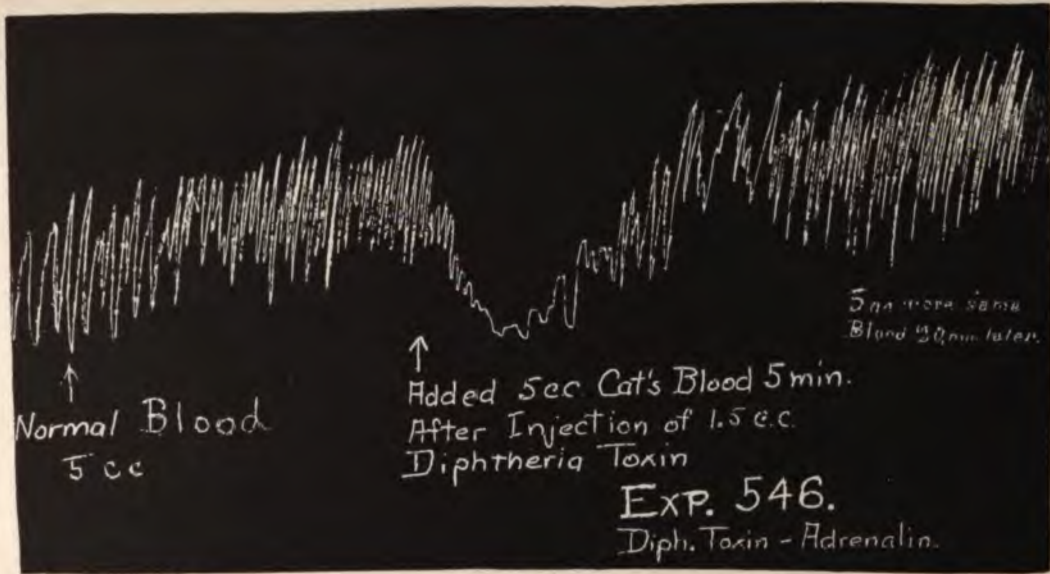
A. B.

FIG. 38. — TRACING SHOWING EFFECT OF SKATOL ON THE ADRENAL OUTPUT OF A DOG. (Cannon Test.)

The first tracing — A — was made by the contractions of intestinal muscle in blood from a normal dog. The second tracing — B — shows the partial inhibition of the contractions produced by the substitution of blood after the injection of skatol, evidencing the presence in the blood of an increased amount of adrenin.

in exertion, in traumatic shock; in asphyxia; in deep hemorrhage; and during the inauguration of the phenomena of death from any other cause.

The biologic test for adrenin was negative — i.e., *functional activity of the adrenals was apparently not excited — in every instance in which the above activations*



A. B. C.

FIG. 39. — TRACING SHOWING THE EFFECT OF DIPHTHERIA TOXIN ON ADRENAL OUTPUT OF A CAT. (Cannon Test.)

The first tracing — A — was made by the contractions of intestinal muscle beating in blood from a normal cat. These contractions were inhibited almost entirely by the substitution of blood from the same cat after the injection of diphtheria toxin — B. After twenty minutes the increased adrenin evidenced by B was oxidized and the intestinal muscle resumed its contractions as in normal blood.

were given subsequent to a division of the nerve supply to the adrenals or subsequent to deep morphinization.

The Relation of the Thyroid to Energy Transformation

Although activity of the thyroid is not attended by striking histologic changes, and while as yet there is no available test by which to determine the presence of thyroid secretion in the blood, there is other evidence which proves that the thyroid plays an important rôle in the process of energy transformation. It is known that the specific activity of the thyroid is dependent on the presence of iodin in combination with certain proteins in the colloid material of the gland, from which it is apparently mobilized by activating stimuli. As we have already stated in the preceding chapter, Aschoff, Beebe, and others have shown that electrical stimulation of the nerve supply to the thyroid results in a marked diminution in its iodin content. Marine, Beebe and others have shown that the hyperactive thyroid gland in Graves' disease is markedly deficient in iodin content.

The meagerness of laboratory studies, however, is amply compensated by the observations which the surgeon has been able to make on a vast scale, — observations which are as definite as are the results of laboratory experiments. Unlike the brain cells and the adrenals which are securely concealed from the eye of the clinician, the thyroid is plainly visible; and gross changes in it are easily seen. A rich store of clinical evidence exists, which confirms the postulate that both the normal and the enlarged thyroid are stimulated to increased activity by agents that cause functional and histologic changes in the brain, the adrenals and

the liver. The volume of the thyroid is increased in fear, in exertion, in sexual excitation, in infection, and it is notably increased during periods of physiological adjustment, such as adolescence and pregnancy.

Negative evidence of the kinetic function of the thyroid is found in the fact that thyroid deficiency produces an adynamic state, in marked contrast to the excessively dynamic state of hyperthyroidism.

The Relation of the Muscles to Energy Transformation

As for the rôle of the muscles in the transformation of energy for both heat and motion, it is sufficient to point out that in the muscles most of the motion and the heat of the body is produced. In the muscles, then, we find the fourth vital link in the kinetic chain. The muscles move the body, circulate the blood, effect respiration and govern the body temperature.

Work Changes

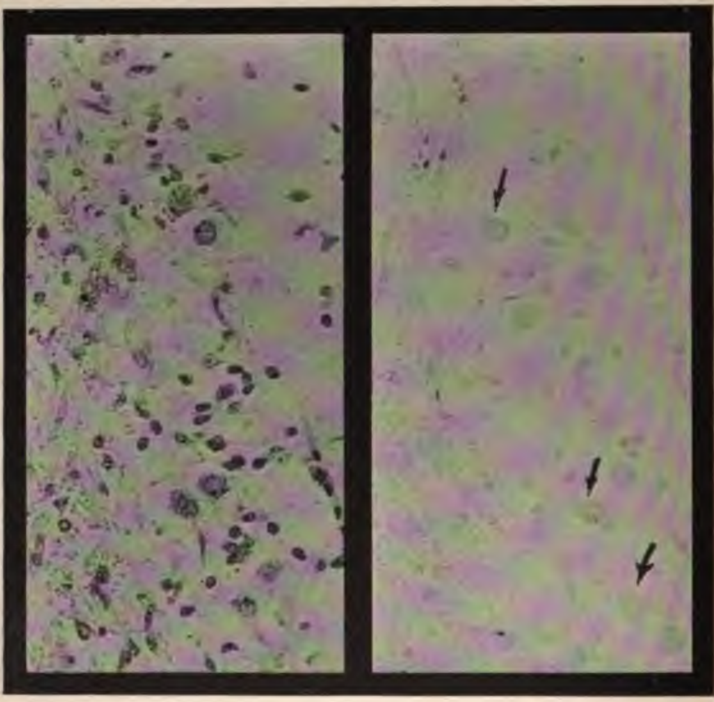
We have seen that every stimulus which produces either heat or muscular activity in the animal body produces morphologic changes in the brain, the adrenals and the liver, and probably changes the iodin content of the thyroid; that no like changes are produced in other organs or tissues of the body; and that these changes are produced primarily or secondarily by the stimuli in question. It is thus a reasonable conclusion that these changes represent *work changes* in the organism. The evidence already presented, however, is not sufficient to prove what that work is, in what capacity each organ assists in its performance,

and whether or not the organs are interdependent in their action.

Let us assume for the moment that the work consists of the conversion of the potential energy stored in the brain cells in the form of chemical compounds — Nissl substance — into electricity, or some similar form of transmissible energy, which on its release activates, among other glands and organs, the thyroid and the adrenals, the secretions of which in the form of hormones activate the brain, which in turn activates the muscles to convert carbohydrates into heat and motion. It happens that we have an interesting analogy to the work changes produced in the brains of animals by the conversion of chemical energy into heat and motion in the conversion of stored energy into electricity in the electric fish. In this fish a part of the usual neuro-muscular mechanism is replaced by a specialized structure for storing and discharging electricity. We found that after a rapid and continuous discharge of their electric energy in response to excitation, the electric fish were exhausted and that their brain cells showed histologic changes identical with those produced in higher animals by muscular work or by heat production. (Fig. 40.) Electricity is a form of energy, and is, of course, convertible into heat or motion. If the discharge of electricity in the electric fish is attended by work changes in its brain-cells, it is not surprising to find work changes in the brain-cells of other animals, as a result of the conversion of their stored energy into heat or motion.

We found further that electric fish could not discharge their electricity when under anesthesia; and

clinically we know that in animals under deep morphia narcosis and under anesthesia the production of both heat and muscular action is hindered or pre-



A. Section of normal cerebellum of electric fish.

B. Section of cerebellum of electric fish after electric discharge.

FIG. 40. — EFFECT OF ELECTRIC DISCHARGE ON THE BRAIN-CELLS OF AN ELECTRIC FISH.

Note the general disappearance of chromatic material and the almost entire disintegration of some Purkinje cells — indicated by arrows — in B, as compared with the definitely outlined cells of A.

(From photomicrographs, × 310.)

vented. In addition our experiments have shown that the administration of morphia before the injection of toxins or drug stimulants minimizes the his-

tologic changes produced by these activating agents, not only in the brain-cells, but also in the adrenals and the liver, while at the same time the body temperature is reduced. We postulate, therefore, that the brain-cells participate as actively in the production of heat as in the production of motion. That is, the brain drives the body in response to the activation of infection or of foreign proteins within the body, exactly as it drives the body in response to an external stimulus which induces the reactions of running or of fighting. The end effect in one case is the production of chemical action and of heat; in the other the production of motion.

If the production of heat, like the production of motion, results from impulses sent from the brain to the muscles, any break in the connection between the brain and the muscles would hinder the production of heat as well as of motion. We know that when nerve connection between the brain and the muscles is nullified by curare, which paralyzes the muscles, or severed by high transection of the spinal cord, the animal is not only deprived of motion, but its heat-producing power is at once on a par with that of cold-blooded animals.[1] That is, with the external application of cold the temperature falls; with the application of heat the temperature rises. When the activity of either the brain or the muscles is depressed or eliminated, therefore, the animal becomes incapable of converting potential into kinetic energy for the production of either heat or motion.

The postulate that the brain cells contribute to the production of heat as well as of motion by sending

[1] Starling.

impulses to the muscles is further supported by the fact that fever may be produced by brain activity alone in the absence of infection and without any visible activity of the skeletal muscles. In experiments in which animals were subjected to fear without any accompanying exertion of the skeletal muscles a rise in temperature was invariably manifested. The temperature of the anxious friends and relatives of a patient will rise while they await the outcome of an operation. In one instance at Lakeside Hospital when a young woman with Graves' disease was undergoing an operation under *anoci association*, the pulse of her waiting mother mounted to 140 and her temperature to 100 degrees, while the pulse and temperature of the daughter showed no change.

The temperature of a patient will frequently rise a degree or more as the result of the visit of a tactless friend who perhaps has exaggerated the danger of the illness or has given vehement expression to her grief. There is a traditional Sunday rise of temperature in hospital wards, where additional visitors are allowed on that day, in spite of the fact that the visitor has brought no additional infection and that the patient has made no muscular exertion. In a ward in Lakeside Hospital containing fifteen children there was an average increase in temperature of one and one eighth degrees as a result of a Fourth-of-July celebration.

In the presence of a fever-producing infection, muscular exertion or other motor stimulation causes additional fever and brain-cell changes greater than would be produced by the infection alone. Apparently, therefore, heat and motion are interchangeable prod-

ucts of the normal interaction of the brain and the muscles, and the coöperation of these organs is essential to the transformation of the potential energy of the body into heat or motion.

Effect upon Energy Transformation of Decreased Activity of Certain Organs of the Kinetic System

A system of organs that coöperate to accomplish a specific function should show as a mark of that coöperation an alteration in the sum total of its activities as a result of any alteration in the condition of any organ in the system. In other words, if the brain, the liver, the thyroid, the adrenals and the muscles coöperate as a system whose chief function is the transformation of energy, then loss or impairment of the function of any one of these organs should result in a loss or impairment of the power of the entire organism to transform energy for the production of heat or motion. In like manner, increased activity of the brain, the adrenals, the thyroid or the muscles should result in an increased production of heat or motion.

Convincing evidence on this point is found in the fact that *adrenin alone, thyroid extract alone, brain activity alone and muscular activity alone are capable of causing the body temperature to rise above normal.* The functional activity of no other organ or gland of the body, alone, and the secretion of no other gland of the body, alone, can cause a comparable rise in body temperature, that is, a comparable increase in the power of the body to convert potential into kinetic energy. No active principle derived from the kidney, the liver, the stomach, the pancreas, the hypophysis,

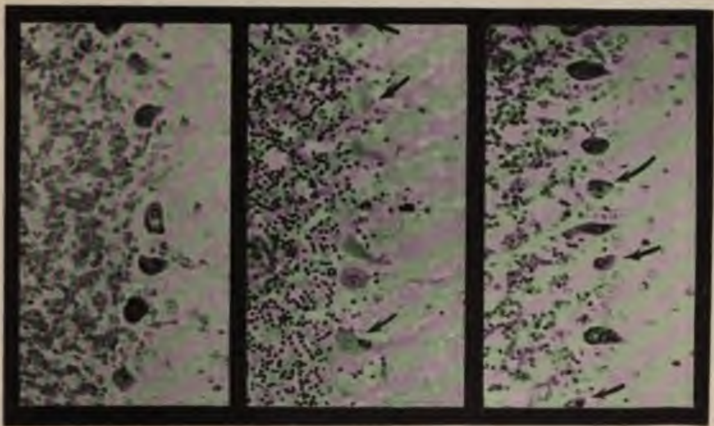
the parathyroid, the spleen, the intestines, the thymus, the lymphatic gland or the bones can, *per se*, cause a rise in the general body temperature comparable to the rise that may be occasioned by activity of the brain or the muscles or by the injection of adrenin or of thyroid extract. On the other hand, when the activity of the brain, the thyroid, the adrenals, the liver or the muscles is eliminated by excision, by narcosis or by anesthesia the power of the body to convert latent into kinetic energy is impaired or lost entirely.

Brain: In certain pathological conditions of the brain, such as cerebral softening, one frequently finds that all the other organs of the body are comparatively healthy. Being physically injured, the brain cannot stimulate the other organs in the kinetic chain to perform their normal rôles; hence the whole process of energy conversion is slowed down. In certain cases of cardio-vascular disease apparently due to an excessive driving of the kinetic system, the condition is cured after the inception of cerebral softening. The brains of the senile show histologic deterioration and the senile exhibit a low range of muscular power and of fever production.

Adrenals: In such destructive lesions of the adrenals as Addison's disease, two of the cardinal symptoms are a subnormal temperature and impaired muscular power. Animals upon which double adrenalectomy has been performed show a striking fall in temperature, muscular weakness *and progressive chromatolysis of the brain-cells.* (Fig. 41.)

Liver: When the function of the liver is impaired by tumors, by cirrhosis or by degeneration, the energy of

the body is correspondingly diminished. This diminution of energy is evidenced in muscular and mental weakness, and in diminished response to all types of stimuli.



A.	B.	C.
Section of normal cerebellum of dog.	Section of cerebellum of dog after adrenalectomy.	Section of cerebellum of dog after repeated injections of adrenin.

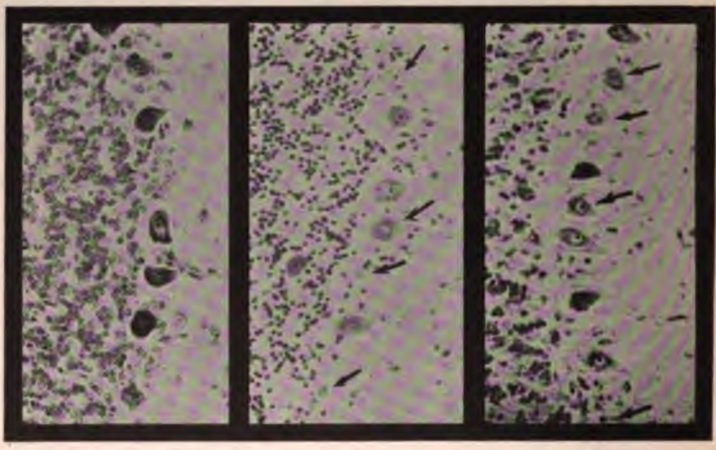
FIG. 41. — COMPARATIVE EFFECTS OF EXCISION OF THE ADRENALS AND OF EXCESSIVE ADMINISTRATION OF ADRENIN ON THE BRAIN-CELLS OF DOGS.

The disastrous effect of withdrawing adrenin from the kinetic system is apparent in B in the extensive loss of chromatic material in all the cells, the disintegration of many and the almost complete degeneration of some cells. The effect of a continuous activation of the system by the excessive administration of adrenin is strikingly shown in C by the large number of hyperchromatic cells, together with evidences of exhaustion and disintegration in some cells. These effects are similar in kind and analogous to the effects produced by withdrawing thyroid secretion or by administering excessive doses of thyroid extract.

(From photomicrographs, × 310.)

Muscles: It has been observed clinically that if the muscles are impaired by long disuse or by a disease such as *myasthenia gravis,* the range of production of both heat and motion is below normal. This is in agree-

ment with the experimental findings that anesthetics, curare or any break in the muscle-brain connection causes diminished muscular action and heat production.



A.	B.	C.
Section of normal cerebellum of dog.	Section of cerebellum of dog after thyroidectomy.	Section of cerebellum of dog after continued feeding with thyroid extract.

Fig. 42. — Comparative Effects of Excision of the Thyroid and of Excessive Feeding with Thyroid Extract on the Brain-cells of Dogs.

The harmful effect of withdrawing thyroid secretion from the organism is shown in B in the high percentage of degenerated cells, the loss of chromatic material and complete disintegration of many cells. The effect of a continuous activation of the system by excessive feeding with thyroid secretion is evidenced in C by the presence of hyperchromatic cells, together with some exhausted, degenerated cells. The cells in both B and C present a marked contrast to the uniform stainability and clearly defined outlines of the normal cells in A.

(From photomicrographs, × 310.)

Thyroid: In myxœdema — thyroid deficiency — one of the cardinal symptoms is a persistent subnormal temperature. Subjects of myxœdema, although prone to infection, show but slight febrile response and succumb

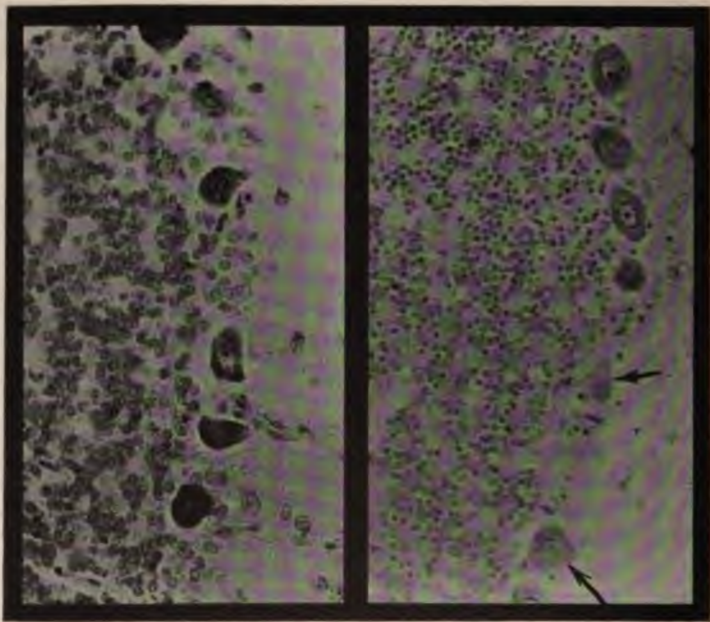
readily. This clinical observation is in striking accord with observations made in the author's laboratory, in which the effect of fear on normal rabbits was compared with its effect upon rabbits whose thyroid glands had been previously removed. While in the normal rabbits fright caused a rise in temperature of from one to three degrees, the rabbits whose thyroids had been removed before the activation made but slight febrile response. Myxœdema subjects show a loss of physical and mental power proportional to the lack of thyroid efficiency. (Fig. 42.)

Effects upon Energy Transformation of Increased Activity of the Several Links of the Kinetic System

In striking contrast to the dullness and torpidity of the myxœdema patient, suffering from depressed thyroid activity, is the supreme excitability and exquisite sensitiveness of the victim of the hyperactive thyroid in Graves' disease, or *exophthalmic goiter.* Here the conditions are exactly reversed. Instead of a sluggish and colorless existence the response to every type of stimulus is exaggerated. The patient having acute Graves' disease responds to toxins, infection, pain or emotional activation by a volcanic transformation of energy that is unequaled in the phenomena of any other known normal or abnormal state.

In the patient with Graves' disease there is a continuous state of exalted consciousness; a tendency to start at the slightest sound, to scream at the slightest pain. The response to contact or chemical stimuli is equally intensified. The heightened activity is seen

in the constant fine tremor of the muscles, in the tendency to the spontaneous production of fever — fever which in fatal cases may mount a degree every hour and reach the incredible height of 109 degrees at the



A. Section of normal cerebellum of dog.

B. Section of cerebellum of dog after injection of iodoform.

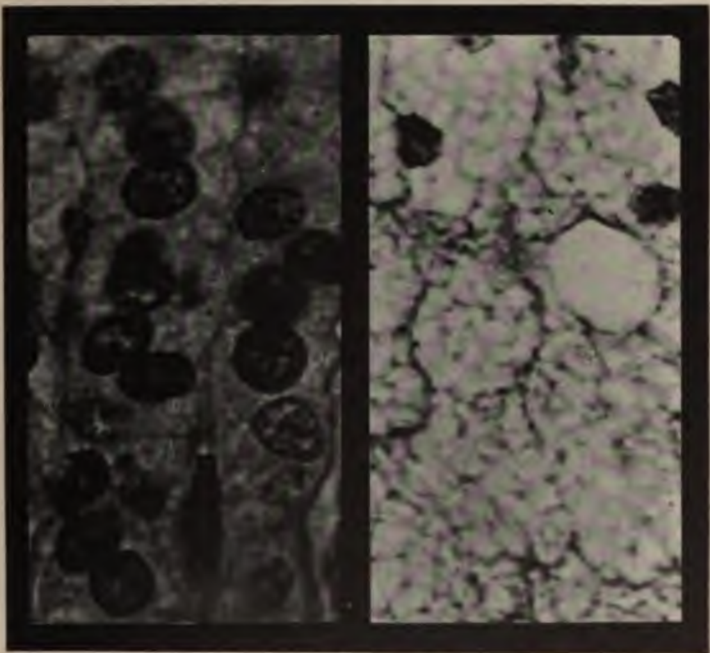
FIG. 43. — EFFECT OF IODOFORM ON THE BRAIN-CELLS OF A DOG.

Note the general disappearance of chromatic material from the cells of B, as compared with the deeply stained, intact normal cells of A.

(From photomicrographs, × 310.)

time of death, a rapidity of rise and a height unequaled in any other condition, pathologic or normal, save in heat stroke. Graves' disease, in fact, presents an unparalleled picture of intensified action of the kinetic

system. In no other phase of health or disease does the thyroid gland appear to manifest so definitely that its rôle is that of *pacemaker* for the kinetic system. In this disease the gland appears to be pouring into



A. Section of normal adrenal of dog.

B. Section of adrenal of dog after injection of iodoform.

FIG. 44. — EFFECT OF IODOFORM ON THE ADRENALS OF A DOG.

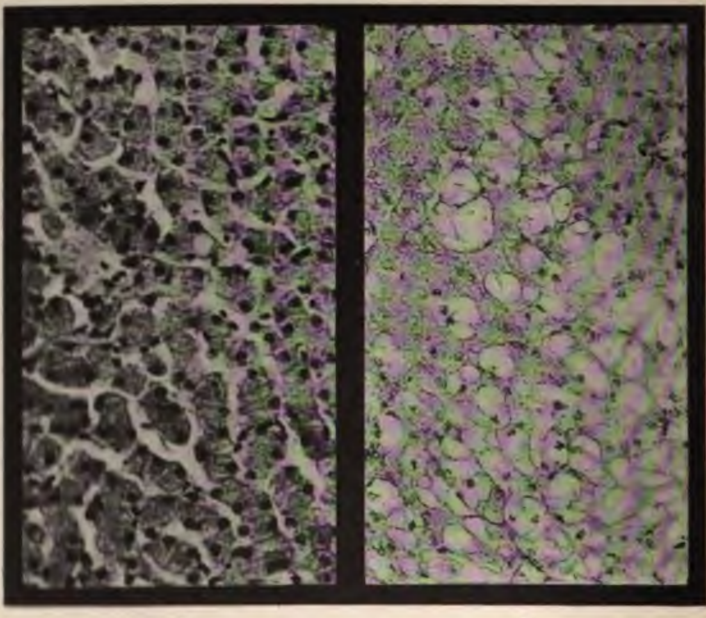
Note the widespread loss of cytoplasm and the vacuolation of some cells in B.

(From photomicrographs, × 1640.)

the blood a continuous secretion which sensitizes the brain, causing it to respond abnormally to environmental stimuli, this activity in turn serving to reëxcite the thyroid and the adrenals, thus completing a vicious

circle of activity which may ultimately drive the mechanism of the patient to destruction.

That the sensitizing agent in Graves' disease is the thyroid secretion is made probable by many facts. The administration of thyroid extract alone or of iodin alone



A. Section of normal liver of dog.

B. Section of liver of dog after injection of iodoform.

FIG. 45. — EFFECT OF IODOFORM ON THE LIVER OF A DOG.
Note the extensive vacuolated areas and the disappearance of nuclei in B.
(From photomicrographs, × 310.)

causes all the phenomena of Graves' disease, except exophthalmos and the emotional facies. (Figs. 43, 44, 45.) Moreover, surgical intervention by ligation of the arteries, division of the nerve supply to the gland and the excision of a part of the gland, or therapeutic treat-

ment by complete rest and the exclusion of all activating stimuli may, singly or in combination, cause a reversion of the picture and restoration to the normal state. And finally, where there is thyroid deficiency, there is the antithesis of this extremely excitable condition — a reptilian sluggishness. Apparently, therefore, by the administration of a diminished, a normal or an excessive amount of thyroid secretion, we can at will produce an adynamic, a normal or an excessively dynamic state of the organism. Through thyroid influence the brain threshold is lowered and life becomes exquisite; without its influence the brain is an inert mass.

The influence upon energy conversion of hyperactivity of the brain, the muscles or the adrenals is no less significant than the effects of hyperactivity of the thyroid. We have noted that brain activity alone can produce fever, and that both voluntary and electrical stimulation of the muscles cause increased temperature; that is, increased energy conversion. In a Marathon race the runner's temperature may rise two degrees, and at the end of a heat, the temperature of a racing horse may show an increase of four degrees. In both instances the conversion of energy is above normal. After a high fever the muscles show a marked impairment of their power to produce motion, suggesting that during the fever they have been involved to an abnormal degree in the transformation of energy.

We have already presented ample evidence of the effect of an increased activity of the adrenals upon energy transformation. The administration of large doses of adrenin of itself produces fever. We have

seen that in rage and fear a physiological preparation for supreme motor efficiency is secured by an increased output of adrenin, resulting in a mobilization of energy compounds, a diversion of the blood stream to the fighting apparatus and a diminution of fatigue. The significance of this point should not be overlooked.

Adrenin performs all the functions that are performed by the sympathetic nervous system except one. Adrenin raises the blood pressure, accelerates the respiration and slows the heart action, governs the output of glycogen from the liver, inhibits intestinal contractions, widens the alveoli of the lungs, increases oxygen combustion in the muscles, dilates the pupils, causes uterine contractions, erection of the hair and sweating. We have shown that it mobilizes the Nissl substance in the brain and directly activates the brain. In short, adrenin causes all the leading phenomena which are the invariable accompaniments of the production of heat and motion in muscular action, infection or emotion, and which are presumably outward manifestations of the processes by which these transformations of energy are effected. The only function of the sympathetic nervous system which adrenin does not perform is stimulation of the adrenals themselves to greater activity.

Interdependence of the Brain, Thyroid, Adrenals, Liver and Muscles

We have seen that the brain and the muscles are interdependent in the production of both heat and motion, since the elimination of either causes a diminution or loss of these processes. We have seen that the

brain and the thyroid also are mutually active in the conversion of energy, and that without the thyroid the brain is impaired. We have seen also that adrenal activity invariably accompanies the transformation of energy, and that increased adrenal activity is prevented when the connection between the brain and the adrenals is interrupted. In other words, our experiments have shown that every adequate stimulus which causes brain-cell changes and which is sufficient to cause the production of motion or heat in the organism, causes increased adrenal activity and histologic changes in the adrenals, except when the adrenal nerve supply has been divided, in which case the application of kinetic stimuli causes neither increased adrenal activity nor histologic changes in the adrenals. Furthermore, when an animal is deeply narcotized with morphia before the administration of a kinetic stimulus there is no increased output of adrenin and there are diminished histologic changes in the adrenals. This evidence seems sufficient to warrant the conclusion that the adaptive activity of the adrenals is largely if not wholly dependent upon the brain.

Is the converse true? That is, is the relation between the adrenals and the brain reciprocal? In crossed-circulation experiments[1] we proved that adrenin alone causes increased brain activity, manifested by increased blood-pressure and hyperchromatism of the brain-cells in the animal whose brain received the adrenin. (Figs. 46, 47.) Animals whose adrenals

[1] In these experiments the circulations of two dogs were cr
so that all the blood from the body of one passed through th
of the other and *vice versa*.

have been excised apparently show no hyperchromatism in the brain cells after the injection of strychnin, toxins, foreign proteins, etc. That is, not only is there no adrenal activity in response to activation after the interruption of nerve connection between the brain and the adrenals, but there is also diminished activity.

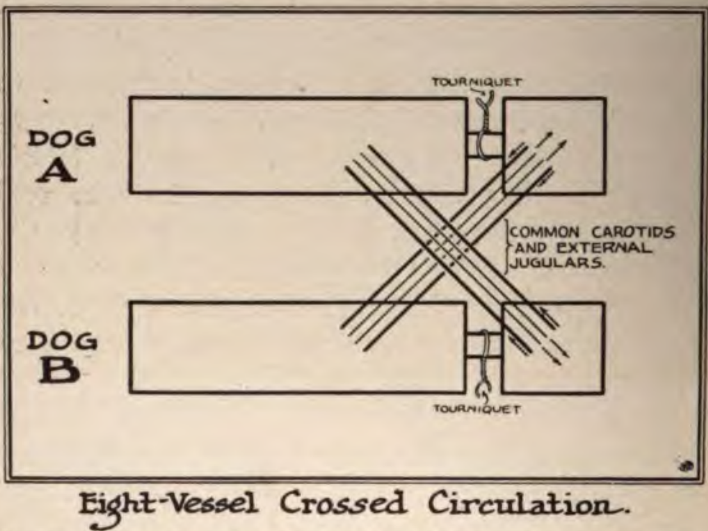


FIG. 46. — SCHEMATIC DRAWING SHOWING COURSE OF BLOOD STREAMS OF TWO DOGS WITH EIGHT-VESSEL CROSSED CIRCULATION.

The circulation of two dogs were crossed in such a way that the head circulation of one dog was anastomosed to the body circulation of the other, and the body circulation of the first dog to the head circulation of the second. A cord encircled the neck of each so firmly that the vertebral and anastomosing circulation was efficiently blocked.

Excision of the adrenals causes death on an average within fifteen hours, during which time there is a steady diminution in Nissl substance in the brain-cells, and a steady fall in temperature and a diminution of muscular power to the vanishing point.

The strong affinity of the brain-cells for adrenin,

which was clearly manifested in our experiments, leads us to think that the Nissl substance may be a volatile — extremely unstable — combination of certain

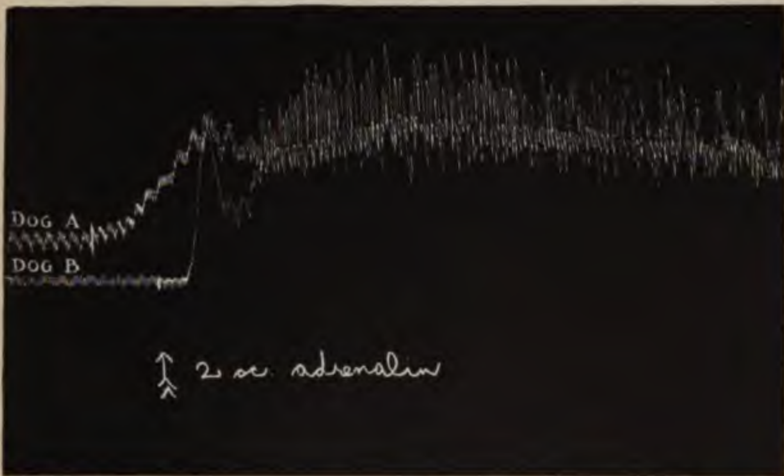


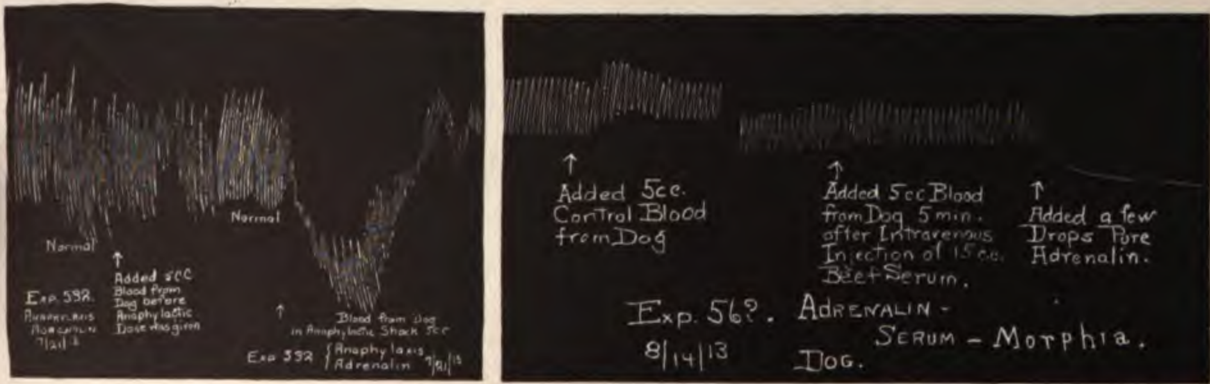
FIG. 47. — BLOOD-PRESSURE TRACINGS CONTRASTING THE EFFECT OF ADRENIN ON THE BLOOD-PRESSURE OF A DOG WHOSE BRAIN ALONE RECEIVED ADRENIN WITH THE BLOOD-PRESSURE OF A DOG WHOSE TRUNK ALONE RECEIVED ADRENIN.

The blood-pressure, taken from the carotid artery of Dog B, *whose brain alone received the stimulus*, its body circulation being anastomosed to the brain of Dog A, *which received no stimulus*, showed a sharp and immediate rise. The blood-pressure of Dog A, *whose trunk alone received the stimulus* (see schematic drawing, Fig. 46), rose later, but to a lesser degree. The rise in blood-pressure of Dog B is probably due to the fact that adrenin acts directly upon some part of the brain, causing it to send energizing impulses to the blood vessels of the body, which result in a rise in blood-pressure.

An interesting feature of the rise in Dog B was its unusual duration, as compared with the rise in an intact animal given an equal amount of adrenin. The brain-cells of Dog B showed hyperchromatism — the inference being that this hyperchromatism is an evidence of increased activity.

Injection of strychnin causes hyperchromatism of the brain in intact animals; but injection of strychnin in animals whose adrenals have been removed causes no hyperchromatism in the brain. Injection of strychnin causes an increased output of adrenin. Perhaps the hyperchromatism caused by strychnin is produced indirectly by its mobilization of adrenin.

elements of the brain-cells and adrenin. The cells of the adrenals do not take the Nissl stain, and the



A. B.

Fig. 48. — Tracings Illustrating Protective Effect of Morphin in Anaphylactic Shock. (Cannon Test.)

In A the adrenin which appears in the blood as a result of *anaphylaxis* inhibits the contractions of the intestinal muscle. Tracing B shows that the injection into a morphinized animal of beef serum, which in the normal animal would have caused a strong anaphylactic reaction and a greatly increased output of adrenin, causes no increased output of adrenin as is evidenced by the contractions of intestinal muscle as in normal blood. Since morphin acts directly upon the brain, this experiment evidences not only the protective effect of morphin, but also the dependence of the adrenal upon the brain for its activity.

brain deprived of adrenin does not take the Nissl stain. The consumption of the Nissl substance in the brain-cells is lessened or prevented by morphia, as is the output of adrenin (Fig. 48); and the consumption of the Nissl substance is also lessened or prevented by nitrous oxid. Both morphia and nitrous oxid act through their interference with oxidation. We conclude, therefore, that adrenin can unite with the brain-cells only through the mediation of oxygen.

In this interrelation of the brain, the thyroid and the adrenals, we have what is, perhaps, the master key to the automatic action of the body; that is, through the special senses environmental stimuli reach the brain and cause it to liberate energy, which in turn activates certain other organs and tissues, among which are the thyroid and the adrenals. The increased output of thyreo-iodin, by facilitating the transmission of electric currents through semi-permeable membranes, increases the passage of nerve impulses and sets the pace for energy conversion. In consequence the adrenals are driven to increased activity, and the increased adrenin in turn excites the brain to still greater activity, as a result of which, again, the entire sympathetic nervous system is activated, as is manifested by the increased heart action, more rapid respiration, raised blood-pressure, increased output of glycogen, increased power of the muscles to metabolize glycogen, etc.

If the foregoing conclusions be well founded, we should find corroborative evidence in histologic or functional changes in that great storehouse of potential energy and neutralizer of the acid by-products of energ

transformation — the liver — in every case in which the brain, the thyroid, the adrenals and the muscles exhibit changes.

Relation of the Liver to Energy Transformation

In our experiments we found that all adequate stimuli which affected the brain, the thyroid and the adrenals produced constant and identical histologic changes in the liver. The amount of glycogen in the liver was diminished in every instance in which the brain-thyroid-adrenal activity was manifested. The duration of life after excision of the liver is about the same as after adrenalectomy — from several to twenty hours. On the contrary, when the administration of adequate stimuli which ordinarily cause histologic changes in the brain, the liver and the adrenals was preceded by deep morphia narcosis, by excision of the adrenals, by interrupting the adrenal nerve supply, there were no histologic changes produced in the liver and the sugar content was normal. This point was demonstrated by the following experiment: An intravenous injection of diphtheria toxin was given to each of a number of rabbits. In each of an equal number of rabbits the intravenous injection of an equal dose of diphtheria toxin was preceded by a large dose of morphia. After four hours all the animals were killed and complete autopsies made. Histological examinations of the organs of the animals which had received the diphtheria toxin alone showed striking changes in the brain, the adrenals and the liver, while in the animals in which the injection of diphtheria toxin was preceded by a large dose of morphia, there

were very slight or no histologic changes in the brain, the adrenals or the liver.

It might be questioned whether the control of the adrenals and the liver exerted by morphia is through its action on the brain or by direct action on the two other organs. Since morphia inhibits brain activity and since severing the nerve connection between the brain and the adrenals also inhibits adrenal action and prevents histologic changes in the adrenal and the liver, it seems probable that morphia controls the adrenal output. Granting that morphia can prevent activation by adrenin, the question arises whether or not it can prevent the action of adrenin injected intravenously. That is, can opium neutralize the effects of adrenin *per se?* On experiment, we found that opium could not prevent the action of adrenin injected intravenously, since under deep morphinization injections of adrenin still caused an increase in the force and the frequency of the heart beat, a rise in the blood-pressure and an acceleration of the respiratory rate. We conclude, therefore, that while opium cannot prevent the *action* of adrenin *per se,* it can prevent the *fabrication* of adrenin by the adrenals. We know clinically that the activity of the thyroid is controlled by large doses of opium. It is known that adrenin measurably governs the functions of the liver; that indirectly the fabrication of adrenin, in part at least, is governed by thyreo-iodin; that *directly or indirectly* the output of thyreo-iodin is controlled by the brain; and that the brain is controlled by morphia. Indirectly, therefore, morphia would be expected to prevent histologic changes in the liver due to emotion, to toxins, etc.

From all this evidence we conclude that the brain, the thyroid, the adrenals, the liver and the muscles are mutually dependent upon each other for the conversion of latent into kinetic energy. Each is a vital organ; each equally vital. While it may be said that excision of the brain causes death in less time than excision of the liver or the adrenals, this statement must be modified by our definition of death. After the entire brain of an animal has been removed by decapitation, its body may live on for eleven hours or more, if the circulation be maintained by an over-transfusion of blood. An animal may live for weeks or months after excision of the cerebral hemispheres and the cerebellum, while an over-transfused animal may live many hours or even days after destruction of the medulla. It is possible, therefore, that, in this sense, the brain actually is a less vital organ than either the adrenals or the liver.

Summing up our evidence in regard to the principal factors in energy transformation, therefore, we have the fact that if communication between the brain and the muscles, the brain and the adrenals, the brain and the thyroid or the brain and the liver be severed, the power of the body to transform latent into kinetic energy for heat or motion is diminished. The body without the brain, the thyroid, the adrenals or the muscles can make little or no response to environment; little or no febrile response to infection. After excision of the brain there is an immediate fall to a low degree of energy transformation in the body, accompanied by no histologic changes in other organs or tissues, showing that without the brain there is no activation.

After excision of both adrenals, there is a rapid decline in the power of the body to transform energy, accompanied by progressive histologic changes in the brain-cells and followed by death. Animals whose adrenals have been excised behave as if at the time of excision the body contained a certain amount of adrenin and as if death followed naturally when this amount had been utilized. After excision of the liver there is, until death, an immediate and progressive loss in the ability of the organism to transform energy, accompanied by marked and widespread histologic changes in the brain-cells. It would appear that the activity of the liver produces in the body a certain margin of safety by which the body is protected against acidosis for a brief time after the liver has been excised, death occurring when this margin is passed.

The excision of no other organ in the body interferes with energy transformation as does the excision of the brain, the adrenals or the liver. Excision of the hypophysis causes diminished muscular power and a subnormal temperature, but a far more gradual decline in energy transformation, since an animal so treated may live for several days or weeks. Excision of the thyroid causes diminished muscular power and heat production in most animals. Excision of the parathyroids may occasion clonic spasms, indicating excessive energy transformation. Neither excision of the thymus nor splenectomy is attended by any notable alteration in energy transformation. Excision of the pancreas leaves protein metabolism undisturbed but interferes with sugar metabolism, to that extent only interfering with energy transformation.

Excision of any part of the stomach or of the intestines is not followed by any change in energy transformation. Excision of the testicles, the uterus or the ovaries prevents the rhythmic changes in energy transformation incident to procreation, but the power of energy transformation for physical exertion or heat production remains unaltered. Excision of one kidney causes no notable change in energy transformation, the damaging effect of excision of the kidneys being due to the accumulation of the by-products of energy transformation. In short, the excision or impairment of no organ, excepting the brain, the adrenals and the liver, causes an immediate and notable change in the histology of the brain, the adrenals or the liver, or in the power of the body as a whole to transform energy, except where some specific process for which one of these organs is directly responsible is concerned. We conclude, therefore, that only the brain, the thyroid, the adrenals, the liver and the muscles are chiefly concerned in the transformation of energy.

In this conception we find a possible explanation of many normal and pathological conditions — one which possibly may point the way to new and more effective therapeutic measures.

PART III

BIOLOGIC INTERPRETATION OF PHENOMENA OF HEALTH AND DISEASE

CHAPTER VII

DISEASES OF THE KINETIC SYSTEM

THE postulate that there is in the body a kinetic system, consisting mainly of certain organs, which are driven by the stimuli of the outer and the inner environments of the body, throws light upon many problems of the medical clinic, as well as of human relations. According to this postulate, the body is a mechanism integrated and driven by the brain in response to adequate stimuli — contact, distance and chemical — arising within and without the body. The phenomena of health and of disease are manifestations of the activity of this system. When the body mechanism is driven at a moderate speed by an environment to which the capacity of the body is perfectly adjusted, the result may be compared to that following the driving of any other machine by a careful and considerate master — a maximum of work done, with a minimum of wear and tear on the parts. When for a short period of time or continuously the driving is at an excessive pace, there results a sudden or gradual breakdown, involving always the weakest link in the mechanism.

When the kinetic system is driven at an overwhelming speed by such activations as severe physical injury, intense emotional excitation, perforation of the intestines, the pointing of an abscess into new territory, the sudden onset of certain infectious diseases, such as

cholera, an overdose of strychnin, a Marathon race, a grilling fight, foreign proteins, or anaphylaxis, there results a condition of acute exhaustion, clinically recognized as shock, and designated, according to its precipitating cause: *traumatic shock, psychic shock, toxic shock, infection shock, anaphylactic shock, drug shock*, etc. Whatever the cause, the essential pathology of shock is identical as is the immediate clinical picture, and the subsequent slow, halting recovery of strength and function.

If instead of a single intense overwhelming activation there is a *continuous* abnormal activation of the kinetic system by one or more stimuli, there is produced a condition equivalent to *chronic shock*, resulting in either a diminished or an excessive activity of some one or more organs. According to the particular organs involved, and the manner of their involvement, this condition may be clinically designated: *nervous exhaustion, neurasthenia, insanity, Graves' disease, myxœdema, goiter, cardiovascular disease, diabetes, Bright's disease, apoplexy or acute acidosis*. In the pathology of all these diseases we may find facts which indicate that they are closely similar in origin, course and treatment.

If, as rarely happens, no part of the organism is weakened or broken by the strain of continuous excessive activation, the unusual spectacle of excessive energy transformation is presented in a human mechanism which outstrips its fellows and crushes its competitors — one of the most amazing sights that life has to offer. Napoleon presented such a spectacle. We may well suppose that Cæsar and Alexander

were such mechanisms. Catherine the Great and Cromwell undoubtedly were cast in a like virile mold. Many of our conquerors, captains of industry and leaders in the professions have been such dynamic mechanisms. But the phenomenon is as rare as it is marvelous. Even where victory is consummated, and usually long before, the mechanism, continuously subjected to heavy stress, shows the effects of strain in the weakening of some one link, less hardy than the rest, and "disease" results from the destruction of the balance of the beautifully adjusted machinery of normal man.

Perhaps this weakening may come first in the brain, from whose depressed activity there results a slowing down of the whole mechanism for the transformation of energy and a lessening of strain on other parts of the organism. Such a general effect is seen after the excessive loss of cortical and cerebellar brain-cells as a result of excessive emotional or physical strain, or of infection, auto-intoxication, injury or any other kinetic drive. In some individuals the strain of over-activation is first indicated by an increased activity of the thyroid gland with a consequent increased driving of the whole mechanism in Graves' disease. Or the liver may be unable to bear the strain, and its inability to break down the acid by-products of energy transformation may cause structural changes in the kidneys or may act indirectly as one of the causes of cardiovascular disease. It is known that cardiovascular disease may result from acute or chronic pyogenic infection, from auto-intoxication, from overwork, from chronic emotional excitation or from the combination of two

or more of these causes. It is known that exophthalmic goiter may follow in the wake of an unfortunate love affair; of a long strain of anxiety in connection with the illness of a relative; of overwork and worry; and that it may result from acute or chronic infection or from intestinal auto-intoxication. It is known that chronic intestinal stasis, with the resultant absorption of toxins, may cause neurasthenia, goiter or cardio-vascular disease.

Not only are the positive effects of organic activity, as seen in disease, explained by the kinetic theory, but the action of certain forms of treatment, by which the organic effects of intense kinetic activation are modified or prevented, may be explained on the same basis. These forms of treatment reduce the activity of the kinetic mechanism as a whole by limiting the activity of some one link in the kinetic chain, thus establishing a condition of inertia or negation to response which is eminently conservative of energy and restorative in effect. Thus traumatic shock can be minimized or prevented by blocking the nerves between the brain and the field of operation by local anesthesia, thus preventing the activation of the brain by harmful traumatic stimuli. In like manner, by depressing brain activity, deep morphinization minimizes or prevents toxic shock and the systemic phenomena of acute infections. This principle accounts for the fact that exophthalmic goiter, one of the principal kinetic diseases, is modified or cured by lessening the activity of the thyroid gland, by the ligation of one or more blood vessels of the gland, or by the excision of a lobe, by severing the sympathetic nerve supply to the gland, or, without

operation, by as far as possible excluding kinetic stimuli, whether of psychic, toxic or dietetic origin. On the same principle may be explained the facts that cardiovascular disease is mitigated by morphia, and that certain forms of opium are beneficial in diabetes.

There is some clinical evidence that some cases of idiopathic epilepsy, a remarkably strong kinetic activation, may be modified but not cured by weakening the kinetic chain by excision of one adrenal and perhaps of a part of the other adrenal, division of the nerve supply of the thyroid, excision of a part of the thyroid and resection of the sympathetic nerve trunks in the neck. The purpose of this operation is to diminish the manifestation of epilepsy, but in addition one result is an increase of sugar tolerance. If we can at will increase sugar tolerance, might not such an operation be of value in the treatment of diabetes? Indeed, on *a priori* grounds, such an operation should improve any chronic disease in which the use of opium gives temporary relief.

In addition to these facts taken from the medical clinic, we have a remarkable array of data drawn from the larger but no less reliable clinic of life itself, which shows that many of this large group of diseases which we have termed *kinetic diseases* because they are obviously aggravated, if not produced, by agencies which activate the kinetic system, are not only often modified, but frequently cured, and, in some instances, actually prevented, by circumstances of life, by states of mind, by habits and by forms of treatment which, like *anoci association* in the surgical clinic, operate by diminishing the number and intensity of adequate brain stimuli.

In truth some of our most interesting evidence regarding the workings of the kinetic system is found in the great clinic of life itself — in contemplating the long list of human ills brought about, admittedly, by "wrong ways of living," and in the tendency of many harassed and overburdened individuals to seek relief from activation in any form of treatment, habit or amusement, which may *prevent the activating integration*, just as in a surgical operation local anesthesia prevents the integration to self-defensive struggle and thus saves the brain-cells from self-destructive activity. In observing the benefits derived by certain sufferers from "faith cures," "mental healing" and other cults, we find most valuable suggestions for the formulation of methods by which the kinetic system may be controlled under certain conditions.

The Adequate Stimulus of Emotion

Chief among the agencies which activate the kinetic system are muscular exertion and emotion. Excessive activation from one or both of these sources is by far the most frequent cause of chronic shock. In the picture of the effects of prolonged fear on the rabbit organism, we have, in epitome, a picture of that constant unequal struggle between the organism and the ever changing environment, which is the fundamental explanation of the fact that the whole fabric of human relations — the chafe and grind of poverty, disappointment, grief, thwarted ambition, unhappy love affairs, loneliness, distrust, envy, competition, heavy business responsibilities, anxiety, uncertainty and worry, as well as their opposites, joy, hope, faith,

realization of ambition, and affection — has a tremendous influence upon the conditions that sustain or destroy life.

As we have seen, emotion is the physiological preparation of the entire organism for the production of one or another of the great primary motor acts of running, fighting or procreation. In the consequent activation there are thrown into the blood stream large amounts of internal activating secretions and glycogen, intended for consumption in the muscles in the production of motion. In addition to this "stoking up" of the blood stream, there is a specific stimulation or inhibition of every organ and tissue in the body, in accordance with the rôle each is to play in the intended adaptive muscular response. Blood is transferred from the parts non-essential to muscular action — the stomach, intestines and genital system — and concentrated upon the machinery necessary to muscular action — the heart, lungs, central nervous system and skeletal muscles. The circulation is accelerated, metabolism is increased; the production of waste by-products is at its maximum; the breath comes faster; the heart beats quickly; the skin is moist from excessive perspiration; the limbs tremble; the extremities tingle; every detail of the intended muscular action is simulated.

In man's early environment there was no break between this preparation for muscular action and its consummation. As a consequence, there was much action and little restraint of action — emotion — just as, to-day, when action ensues precipitately upon a stimulus, there is no manifestation of fear, anger or

sympathy. In the modern environment, where there is a minimum of action and a maximum of restraint of action, *man is in auto-captivity to phylogenetic tendencies.* The consequent excessive and continuous stimulation of the heart and blood vessels, of the brain, thyroid, adrenals and liver, together with the coincident excessive and continuous inhibition of the digestive processes and the accumulation of unused secretions and waste products, leads frequently to certain organic degenerations.

An interesting phenomenon, from a biologic viewpoint, is the fact that it is in man more often than in woman, that increased energy transformation leads to cardiovascular disease, diabetes and nephritis. Man, more than woman, is subject to cardiovascular and cardiorenal disease; to *thrombo-angiitis obliterans* and to diabetes. Woman, on the other hand, is the more frequent sufferer from diseases of the thyroid gland. In this proneness of woman to diseases of the thyroid and of man to diseases caused by hypertension, we have a curious instance of pathologic modification along lines of adaptation.

The adrenals preëminently control the mechanism for increasing motor efficiency during short periods of increased transformation of energy. The adrenals are the organs most heavily involved in muscular work. On the other hand, the thyroid controls the mechanism which regulates energy transformation during longer periods of increased activation. It is known that the thyroid enlarges during sustained periods of increased activity, especially during infection, adolescence and pregnancy. Throughout the ages of evolution, the

male has been chiefly the motor member of the family; he has been, not exclusively, but for the most part, the hunter, the fighter, the searcher for food, — activities which have required increased transformation of energy during short periods of time, with proportionally heavy demands upon the acid-neutralizing mechanism of the body. The female, on the other hand, has borne the burden of procreation and of the lighter but more constant domestic tasks, and has been correspondingly dependent upon the mechanism for sustained physiologic efficiency, represented chiefly by the thyroid. This age-long differentiation may conceivably have led to a corresponding differentiation in the physiologic expression of emotion, with a corresponding differentiation in the diseases caused by emotion. According to a striking statement made by Loeb, "Man and woman are, physiologically, different species."

Often, before any one of the more serious diseases resulting from excessive driving of the mechanism is apparent, a warning may be discerned in the onset of some lesser disturbance, such as chronic dyspepsia, auto-intoxication, disturbances of the skin, the teeth and the hair. The increased amounts of unused secretions and of by-products of activity tax all the organs of elimination, including the skin. It is not surprising that the skin of many highly emotional but "intelligent" persons, in whom we presume control and repression, should exhibit a stained and sallow appearance, should become odorous and oily, or cold, moist and covered with unsightly blotches and pimples. The skin of virtuous girls, subjected to the continuous

emotional strain of a long engagement, often presents such an appearance. The transformation that takes place after marriage may be striking. Indigestion disappears; the appetite returns; metabolism increases; the cold, clammy, sticky, yellowish, pimply skin is replaced by a soft, pink, warm, velvety covering.

Dentists affirm that under continued strong emotion the character of the saliva changes, pyorrhea tends to develop and teeth rapidly decay. That emotional strain may cause the hair to turn gray prematurely and to fall out is a common tradition, not unsupported by fact.

If emotion, particularly fear, causes such far-reaching metabolic disturbances, why does it not produce even more baleful consequences? Indeed, why has not emotion wrecked the race? Is it because there are now certain agencies at work in society, which hold in check this harmful tendency, as immunity and phagocytosis protect the organism against bacterial menace, and as the custom of wearing clothes and building houses is a protection from the dangers of wind and cold and hostile strangers? Has there been evolved in man some counter-adaptation which provides a partial protection against self-destruction from the too long retained motor adaptation which we term "emotion"?

Fear versus Faith

In attempting to find an answer to these questions, we are led to contemplate the fact that physical benefit is derived from those factors in life, which solace and reassure the mind, which "rejuvenate the spirit,"

which dispel worry, and which substitute faith and tranquillity of mind for turmoil and terror. Many attempts have been made to explain the universal desire for joy and recreation, for entertainment, for diversion, for any activity or mental influence, which changes the integration, "diverts attention" from the work at hand, supplies a new field of interest or closes the mind to all interest. It would seem that a key to these phenomena might be found in the very fact that emotion has the power to harm the organism. On the principle that fear causes the dissipation and faith the conservation of potential energy, we can understand the far-reaching and abiding benefits of religion in all ages, among all peoples, throughout the whole human race, as far back as we have any record. We can understand the power of prayer and of belief in a Supreme Being who is also Redeemer and Solace, to put "new life" into the discouraged and faint-hearted, and its overwhelming influence for good upon the weak, oppressed and sick-at-heart. We can understand the power of so-called "faith cures"; of beliefs in fetishes and charms; even of the faith in one's own physician, which undoubtedly plays a part in the successful outcome of most therapeutic measures.

This principle explains the striking benefits in all situations in life of good luck and success, of cheerful and optimistic friends, of congenial occupations, associates and surroundings. It explains the spectacular, successful careers of certain personalities abounding in health, optimism and self-confidence, the value of self-confidence in business, and the wreckage of hopes and fortune which often attends the lack of these qualities.

Since whatever dispels worry and uncertainty helps to stop the body-wide activation which leads to lesions as truly physical as a fracture, we can understand the therapeutic significance of the admonitions to "take a vacation"; "go abroad"; "go fishing"; to do anything that will give a change of scene and occupation. On this basis we can understand the desperate tendency of certain sorely driven organisms to seek forgetfulness in alcohol or narcotic drugs; of others, driven beyond the point of endurance, to settle their problems finally by suicide.

Realizing that sedentary occupations, like suppressed emotion, produce an accumulation of harmful products in the blood stream, we can understand the good feeling that follows a lively game, a long walk or exercise in the open air after working hours, since by these means is accomplished the elimination, by oxidation or otherwise, of much of the superimposed burden. We can understand the overwhelming desire in time of anger or worry to "walk it off" or to "talk it out" with somebody. We can understand the value to the physician of psychic analysis, since it enables him to get at the root of his patient's trouble and to elicit a full confession, which, in itself, brings a measure of relief.

The fact that the lesions wrought by suppressed integrations to activity are largely the same for other animals as for man, explains why the fettered wild animal "pines away" and dies in captivity, or grows "ugly" and "vicious"; and why, when released to liberty and its natural environment, it quickly shows a return to health and good nature. Considering this tendency of the kinetic or dynamic organism to be

destroyed by its own adaptive mechanism, it is easy to see why certain adynamic species, such as the turtle or the elephant, survive longer than animals evolved for intense kinetic activity, such as the deer and the rabbit; why, generally speaking, the expectancy of life is greater for placid individuals than for those of an "explosive" temperament; why the calm adynamic philosopher outlasts the dynamic iron-worker, who, through excessive exertion, breaks early a link in his vital chain; why the timid individual, who thinks his life is threatened by trivial incidents and hence avoids risk and responsibility, outlasts the strenuous and careless-of-self individual, who goes on the rocks just past middle life.

Thus innumerable phenomena of life may be interpreted by applying this principle of the antithetic actions of fear and faith; phenomena not only of the life of the individual, but of the life of the race at large, as manifested in its past history, in political situations of to-day, in family life; phenomena which prove invariably that the conscious processes of life, like the unconscious processes and the passive modifications of the structure itself, are but evidences of nature's mode of securing survival for the species. The processes of "reason" and "instinct," like the "protective muscular reflexes," the pain areas, the phenomena of phagocytosis, immunity and blood clotting, are merely examples of the workings of the system which secures "survival of the fittest." In thus placing faith, hope and charity on the same plane with muscular reflexes, in their power to conserve the life of the race, we but give them their proper place

in evolution as adaptations which have arisen coincidently with the need for such modifications. And furthermore, we place them on the same plane with another "conscious" but no less automatically evolved adaptation by means of which the energy of the individual is conserved — the application of the principle of *anoci association* in surgery.

Whatever weakens or breaks the integration of the body at the brain link, breaks the continuity of the kinetic chain and diminishes the expenditure of energy, and to that extent is a conserver of life. The technique of *anoci association* was the outgrowth of a study of nature's methods of adaptation. It does not seem too much to expect that a further study along the same lines may lead to a further understanding of the relations of fear and faith to the laws of life, as a result of which, through education and training, the principle of faith may fulfill as useful a rôle in the clinic of life as is fulfilled in the clinic of surgery by *anoci association.*

CHAPTER VIII

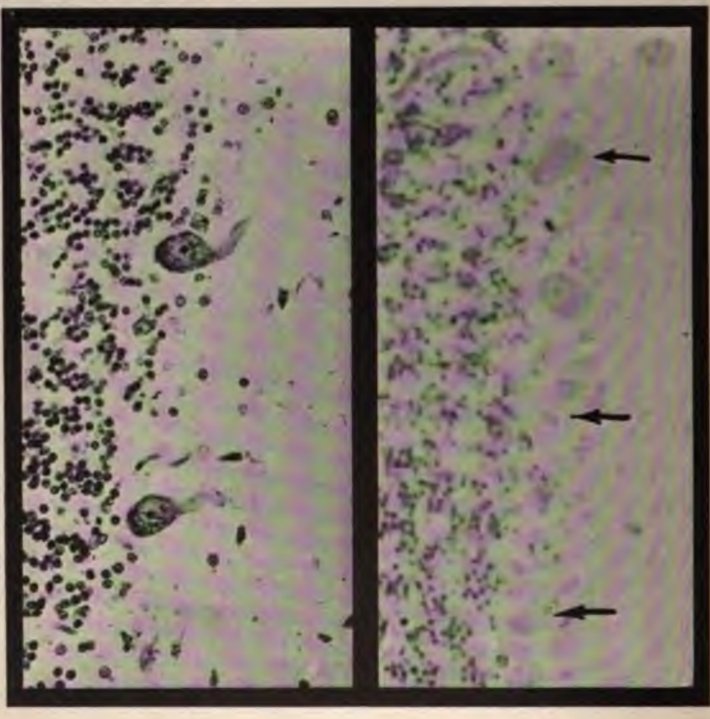
KINETIC DISEASES — *Continued*

Graves' Disease

As in shock the kinetic system is driven to the point of exhaustion by one overwhelming, intense activation, — injury, emotion, strychnin, infection or anaphylaxis, — so in Graves' disease, as we have already stated, the kinetic system is driven by a continuous activation, as a result of which a pathologic interaction is established between the brain and the thyroid, whereby the threshold to all stimuli is kept continuously low. In shock an immediate collapse of every function in the body is exhibited with visible lesions only in the brain, the adrenals and the liver. Graves' disease exhibits a progressive alteration in every function, leading eventually to exhaustion, with visible lesions — depending upon the duration and severity of the disease — in every organ and tissue of the body; not alone in the brain, adrenals and liver (Fig. 49), but in the heart and blood vessels, the muscles, the thyroid, the thymus, the pancreas, the spleen, the lymphatics, the skin, the skeletal muscles, the teeth, the hair and the bony skeleton. Extreme and protracted exhaustion from excessive exertion, excessive emotion or chronic infection causes similar lesions. (Fig. 50.)

In other words, the principal phenomena of Graves'

disease are identical with the leading phenomena of any other kinetic activation of a corresponding duration and degree of intensity. The phenomena of fear,



A. Section of normal human cerebellum. (After accidental death.)

B. Section of human cerebellum after death from exophthalmic goiter.

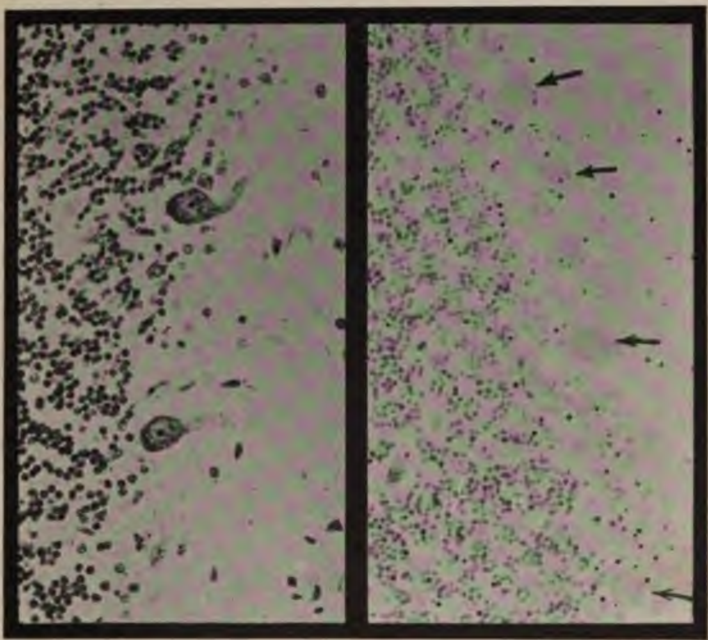
FIG. 49. — EFFECT OF EXOPHTHALMIC GOITER ON THE BRAIN-CELLS OF A HUMAN BEING.

Note the loss of chromatic material in all and the evidences of deterioration in many of the Purkinje cells in B.

(From photomicrographs, × 310.)

anger, sexual excitation, physical exertion as in athletic contests, acute overwork, acute infection — all recapitulate the phenomena of Graves' disease and produce the

same lesions in the brain, adrenals and liver. (Figs. 51, 52, 53.) Conversely, many of these activations cause enlargement or hyperplasia of the thyroid. Thus, fear, anger and sexual love cause temporary enlarge-



A. Section of normal human cerebellum. (After accidental death.)

B. Section of human cerebellum after death from acute septicemia.

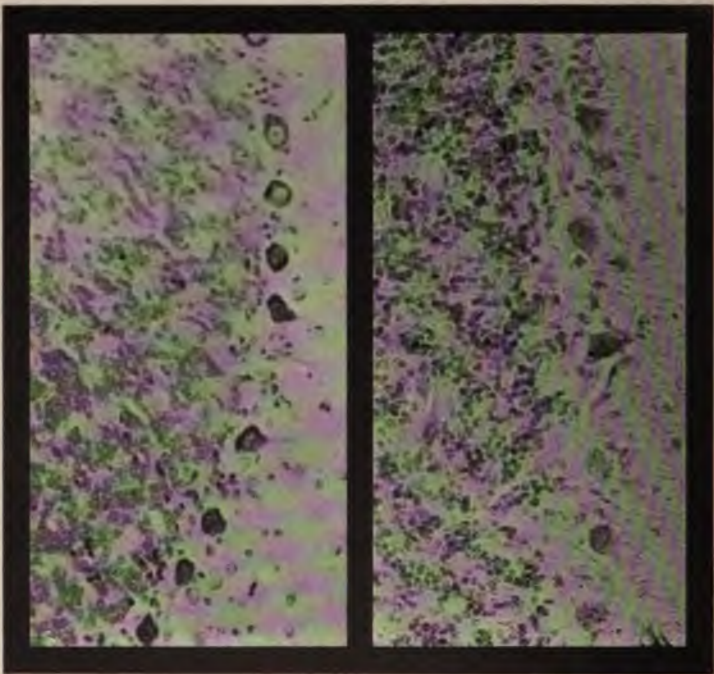
FIG. 50. — EFFECT OF ACUTE SEPTICEMIA ON THE BRAIN-CELLS OF A HUMAN BEING.

A widespread loss of chromatic material and the almost entire disappearance of some Purkinje cells (indicated by arrows) characterizes B, in contrast to the well-stained, intact appearance of the Purkinje cells in A.

(From photomicrographs, × 310.)

ment of the thyroid; there is hyperplasia of the thyroid in pregnancy, in chronic infections and, perhaps, in intestinal auto-intoxication as well.

There is a strong resemblance between certain aspects of Graves' disease, of iodism, of emotion and of infection. The likeness between Graves' disease and all



A. Section of normal cerebellum of cat.

B. Section of cerebellum of cat after infection.

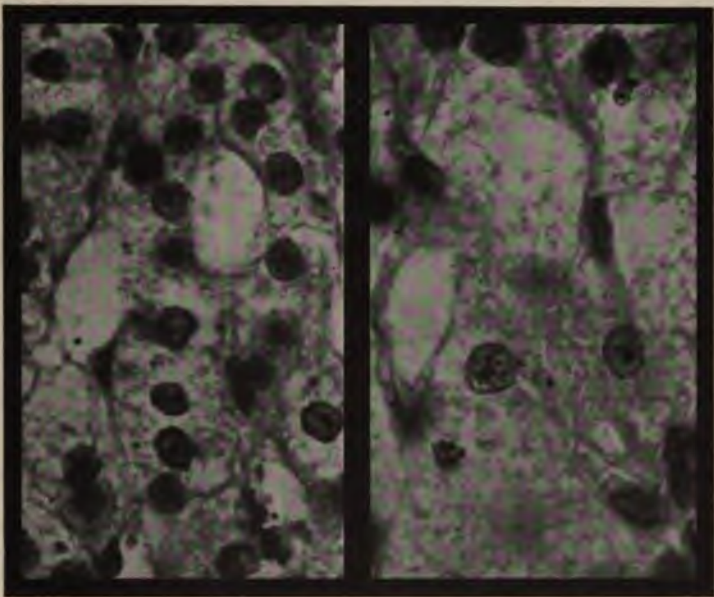
Fig. 51. — Effect of Infection (Streptococcal) on the Brain-cells of a Cat.

Note the marked disintegration of the Purkinje cells in B.

(From photomicrographs, × 310.)

types of excessive emotion is not surprising in view of the frequency with which the disease is traced to a nervous origin. For of all activating stimuli responsible for Graves' disease, chronic emotional activa-

tion and infection are, perhaps, the most dominant. In many cases careful inquiry will disclose some deeply intrenched disturbing emotional factor — a great grief, the existence of harassing home conditions, poverty



A. Section of normal adrenal of cat.

B. Section of adrenal of cat after infection.

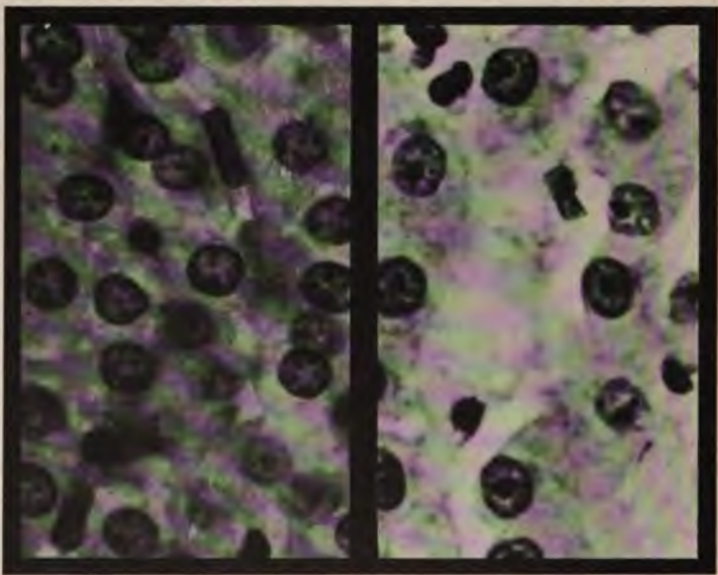
FIG. 52. — EFFECT OF INFECTION (STREPTOCOCCAL) ON THE ADRENALS OF A CAT.

Note the disappearance of nuclei, the general loss of cytoplasm and the vacuolated spaces in B.

(From photomicrographs, × 1640.)

or shame, business reverses, overwhelming responsibilities, an unhappy love affair, or some acutely distressing thought, which drives the kinetic system incessantly. In my own experience, in cases of Graves' disease for the causation of which no factor

in the external environment can be held responsible, the internal environment has usually supplied the disturbing factor, infection or auto-intoxication, for example. I have never known a case of Graves' disease to result from hard physical labor, unattended



A. Section of normal liver of a cat.

B. Section of liver of a cat after infection.

FIG. 53. — EFFECT OF INFECTION (STREPTOCOCCAL) ON THE LIVER OF A CAT.

Note the general disappearance of cytoplasm and the vacuolated spaces in B.

(From photomicrographs, × 1640.)

by "psychic" strain; nor from energy voluntarily and naturally expended.

Whatever the exciting cause of Graves' disease, however, whether unusual business worry, disappointment in love, a tragedy, a strong fear, the illness of a

loved one, intestinal auto-intoxication, an acute or chronic infection, administration of excessive doses of iodin or thyroid extract, the symptoms are identical and closely resemble the phenomena of the great primitive emotions, of acute infection and of muscular exertion.

After chemical stimulation of the body by a foreign protein or an infection, the pulse quickens, the blood-pressure rises, respiration is increased, the temperature is elevated, digestion is inhibited, metabolism is increased and pathologic changes are produced in the organs of the kinetic system which are identical with those produced by emotion or physical exertion. In short, there is a period of hyper-stimulation in fever which exactly corresponds to the period of hyper-stimulation in emotion, and signifies the preparation of the organism for self-defense by chemical activity, just as emotion signifies the preparation of the organism for self-defense by motor activity. It has been proved that the increased metabolism following upon the increased temperature purifies the body partially, at least, in a chemical way by inhibiting bacterial growth and probably in addition by causing a chemical disintegration of toxic proteins into harmless substances which are eliminated.

It would seem, therefore, as if fever were the result of a driving of the kinetic mechanism by a foreign protein or infection stimulus for purposes of self-defense by the splitting up of the molecules of the foreign protein through the transformation of latent energy into heat; and that emotion is the result of a driving of the mechanism by a psychic stimulus for purposes of self-

defense by muscular action. On the other hand, it would seem that Graves' disease is a purposeless driving of the mechanism by some obscure stimulus connected with a pathologic alteration in the function of the thyroid which is, as we have stated, apparently *the pacemaker of the kinetic system.*

That these several activations involve the same mechanism is evidenced further by many other points of similarity between Graves' disease and infections. The likeness of the phenomena of Graves' disease to those of chronic infections, particularly of tuberculosis, is so marked that it is not at all uncommon to find diagnosticians of wide experience recommending treatment for tuberculosis to a patient with Graves' disease and an operation for Graves' disease to a patient with tuberculosis. In two different cases of the same degree of intensity, it is almost impossible to distinguish the case of Graves' disease from the case of tuberculosis. Sometimes, both conditions may be present in the same patient. The following symptoms are common to both Graves' disease and tuberculosis; tachycardia, increased respiration, flushed face, tremors, persistent slight fever, nervousness, rapid loss of weight, digestive disturbances, hyperplasia of the thyroid and of the lymph glands and enlargement of the heart. Even at autopsy the lesions — barring the tuberculosis focus itself — may be so nearly identical in the two cases as to baffle differentiation. In tuberculosis as in Graves' disease, *the entire kinetic system is over-driven.*

Thus, the kinetic theory of Graves' disease, of infection and of emotion supplies a possible biologic interpretation of the induction of these states, of their mutual

resemblance and of the method of their control. All are modified by rest; all are temporarily controllable by morphia; all cause increased H-ion concentration in the blood, and, therefore, tax heavily the organs of acid neutralization, namely, the respiratory center, the kidneys, the adrenals and the liver. *The increased respiratory rate in each of these conditions is accounted for by the specific stimulative effect of the increased H-ion concentration of the blood on the respiratory center.* The demand for neutralization of the increased acidity incident to emotion, exertion, infection or Graves' disease is met by increased activity of the adrenals and liver. If the acidity increases so rapidly that neutralization cannot keep pace with it, then nephritis may result from the action of the acid by-products upon the kidneys. Hence, in emotion, in infections and in Graves' disease, albumin and casts are frequently found in the urine and in extreme cases, acute acidosis may develop. The acidosis of emotion, of infection and of Graves' disease is evidenced in each case by thirst. The cycles of vomiting in Graves' disease are caused by acidosis, which is the most common cause of death in this disease.

It is a significant fact that continued lymphocytosis is common to both Graves' disease and tuberculosis. By the production of lymphocytes the body defends itself against infection. Why, then, the lymphatic hyperplasia, indicative of overwork, in Graves' disease in the absence of infection? It is possible that the protective rôle played by the thyroid in all infections is not that usually assigned to it, — namely, neutralization of bacteria or toxins by direct action of the

thyroid secretion upon the foreign protein, — but through the action of thyroid secretion upon the lymphatics, simultaneously with its effect upon the other self-defensive mechanisms. If this be true, there should be less or no lymphocytosis in infection in an individual with myxœdema or in a cretin. Thus, in the immediate symptoms and in the end effects, even to the resulting acidosis and pathologic lesions, we find a close resemblance in the essential phenomena of exertion, emotion, infection and Graves' disease, a fact which tends strongly to uphold the kinetic theory.

Certain Resemblances between Cardiovascular Disease and Graves' Disease

The analogy between diseases of the thyroid and diseases involving the adrenals is borne out by many clinical points. Certain cases of Graves' disease and of cardiovascular disease present a particularly strong likeness to each other. Each of these conditions bears an intimate relation to foreign protein activation and to "nervous strain." The etiology of Graves' disease is much the same as that of cardiovascular disease if perhaps in the former case problems of the home be substituted for problems of business. In each of these diseases a recall of the unhappy circumstances or conditions which led to or precipitated the acute stage, is sufficient to cause an exacerbation of all its symptoms. The most efficient non-surgical means by which each of these diseases may be modified are rest, diversion, change of scene and occupation. In each the secretion of the more closely related gland seems to bear a specific relation to the production of the disease. For instance,

the cardinal symptoms of Graves' disease may be produced in a normal person by the excessive administration of thyroid extract, and in the patient with Graves' disease the administration of thyroid extract, even in small quantities, causes an immediate exacerbation of the symptoms. In like manner, adrenin, when continuously administered to a normal animal, is said to produce lesions similar to arterio-sclerosis, and it aggravates the symptoms of cardiovascular disease when given to a patient with that disease. Like results cannot be obtained by the administration of the secretion of any other gland in the body. In Graves' disease the thyroid is always enlarged; in cardiovascular disease, the adrenals in many instances are enlarged.

Moreover, since in Graves' disease immediate improvement follows any measure by which the activity of the thyroid gland is depressed, *i.e.*, division of nerve supply, lessening of vascular supply, removal of a lobe, removal of general causes of activation by rest, diversion, change of scene and dietetic control, it is reasonable to suppose that the condition of the patient with cardiovascular disease also would be improved by any means which would depress the activity of the kinetic system — especially of the adrenals. The most efficient treatment now employed in cardiovascular disease consists in depressing cerebral activity by means of prolonged rest, diversion and dietetic control, but it is reasonable to believe that more striking and immediate benefit might be secured by depressing the activity of the adrenals directly by dividing their nerve supply or removing a portion of the glands. This belief is strengthened by the fact that in our

experiments, cats and rabbits, in which the nerve supply to the adrenals had been divided, after recovery from the operation showed no evidence of an increased output of adrenin after intense psychic or toxic activation which in normal animals caused a large increase of the adrenin output. There is as yet no convincing proof that increased activity of the adrenals alone causes cardiovascular disease, but there is evidence that the adrenals play an important rôle in the causation of that disease.

Note on Arterio-sclerosis

The literature on the etiology of arterio-sclerosis is a long record of superlative stimulations and deep depressions — a story of great risks taken and great losses borne; of heavy burdens carried and long strains endured; of vast responsibilities assumed; of excessive dissipations; of chronic infection; of auto-intoxication; of overindulgence in food and intoxicants; of great joys and great griefs; of hopes, anxieties and despair. It is essentially a story of the modern world; of power and progress and success; of liberty and luxury and of their antitheses; of mental tolerance combined with bitter, crushing oppression. The contemplative scholar of the Middle Ages, the bucolic Swede, the wandering Scotch bard, the Italian peasant, probably rarely knew arterio-sclerosis, except as the logical accompaniment of a ripe old age. The director of vast financial enterprises, the man who holds the fates of thousands in his hand, he who carries tremendous physical burdens: the Chinese coolie, the Japanese rickshaw man, the athlete of the western world, the

emotional American, the excitable Jew, the bank president, the *bon vivant*, — these are the men whose days are shortened by early hardening of the arteries; who preëmpt to themselves the cardiovascular and, likewise, the cardiorenal diseases. The superlatively emotional Jew, besides being a frequent victim of cardiovascular disease, is likewise a frequent sufferer from the allied condition, endarteritis obliterans. Among animals the high-spirited wild animals in captivity, the mettlesome race horse, and the dray horse, fretted and driven often beyond its capacity, are frequent sufferers from cardiovascular disease. The somnolent, unfettered cow is exempt.

Note on Thrombo-angiitis Obliterans

The likeness of thrombo-angiitis obliterans (endarteritis obliterans) to cardiovascular disease and other kinetic diseases is shown by many interesting clinical facts. This disease is characterized by a gradual obliteration of the arteries, leading to progressive anemia with dry gangrene of the extremities, first of the digits, then of the feet and hands, and finally of the major portions of the limbs. It occurs in the most active period of life of the males of those races and individuals who preëminently are exponents of the "strenuous life," a high percentage of victims of this disease being found among the Jews. Its early stages are marked by cycles of phenomena which bear a definite relation to nerve strain, to overwork and, particularly, to emotional excitation. The first symptom is a sensation of cold, numbness and tingling in the extremities, being followed, as the disease progresses,

by pain in these parts and not infrequently by headache. In this early stage nitroglycerin often gives temporary relief. Increased psychic strain causes a corresponding aggravation of the symptoms. As the disease progresses, there is continued numbness; the pulsations of the supplying artery become weaker; nutrition fails and slow atrophy of the parts follows. The entire limb behaves as if the blood supply were being gradually and at first intermittently shut off by a clamp — a clamp opened now and again, but finally closed altogether.

In the early stages of certain cases the patient may improve or even recover if he takes a long pleasant vacation or is buoyed up by new hopes and helpful developments in his business. But if the environment is not changed, there is the same inevitable progress to destruction as under the same conditions is induced in Graves' disease, cardiovascular disease or diabetes. The same influences that modify these diseases, in like manner and to the same extent modify thrombo-angiitis obliterans. A return to the original activating environment or a recall of the original harmful stimulus may precipitate a return of the vicious circle.

The tendency to relapse produced by *noci association* (harmful recall) is illustrated by a woman who to a marked degree exhibited the symptoms of this disease. A trip abroad was prescribed and taken; and during three months of pleasant travel, the patient experienced no symptoms. On her return she thought she was well, until one day, while motoring in the city, she saw a man killed by a street car. She directed her chauffeur to drive on, but not before she had caught a glimpse

of the mangled form. The sight was all the stimulus needed to bring an instant return of the familiar symptoms. Within a few minutes, she experienced again the pressure in the head, the headache, the numbness, the coldness and tingling of the feet — all the symptoms from which she had been nearly free for eight months. The symptoms continued throughout the day and passed away gradually.

In all the kinetic diseases environmental stimuli similar to those which caused or bore a part in the causation of the disease tend to exaggerate or — if convalescence is well established — to reproduce the phenomena of the disease. For instance, in a patient with cardiovascular disease any reference to business perplexities — a problem calling for close consideration, a telegram asking for advice or decision upon a proposed business move — is sufficient to recall the activating *noci association*, which was the original source of the disease. The brain of the sufferer presents a low threshold to the specific adequate stimulus. As the steady dropping of water upon the same spot on the surface of the body by summation of stimuli causes gradually increasing pain until the state of exhaustion is reached, so the continued activation of the kinetic system by business cares, by professional burdens, by chronic infection or by emotional strain leads to summation of stimuli and final breakdown.

Note on Bright's Disease

In the great strain laid upon the organs of reduction and elimination by the excessive production of by-products in emotional activation, physical exertion

and infections we may have a key to the cause of Bright's disease. We have shown by experiment that in frightened rabbits, enraged cats and traumatized dogs the kinetic system can be driven at such a rate of speed that the organism is unequal to the task of neutralizing the too rapidly formed acid by-products so that they can be eliminated without injury to the kidneys. In addition, we have shown that when the activity of the brain has been depressed by morphia the rate of transformation of energy is decreased, and the production of acid by-products correspondingly lessened. If, as seems probable, the adrenals and the liver are the most important agents by which the reduction of acid by-products is accomplished, then an habitual failure of these organs to perform this function might lead to an accumulation of harmful compounds, which would directly facilitate tissue degeneration in the kidneys, thus causing nephritis. In Bright's disease hyperplasia of the adrenal glands is frequently seen.

Note on Diabetes

The more powerful excitants of the kinetic system cause an increased output of adrenin, which in turn causes the mobilization of the glycogen stored in the liver so that among other results of excessive kinetic activation, glycosuria is produced. While glycosuria is not diabetes, it may represent a step toward this disease, and one would expect, therefore, that the kinetic drive which in one individual causes a lesion of the thyroid, in another of the brain and in another of the adrenals, might in others produce diabetes. That this is so is

shown by the fact that diabetes is aggravated by the conditions which increase psychic strain, and lessened by conditions which obviate psychic strain. The identification of the common causes of diabetes with the common causes of Graves' disease may explain why in the words of a certain phrase maker, "when stocks go down in New York, diabetes goes up"; why diabetes is more commonly found in large cities, among individuals and races who are constantly under a strain of business perplexities, and who are constantly within sight and hearing of thousands of irritating and harassing episodes; and why it is rare in localities where leisurely and quiet ways of life prevail. In the fact that here, again, the emotional trade-driven Jew is a frequent sufferer, we have pertinent matter for consideration.

Since diabetes not only numbers among its common causes the common causes of other kinetic diseases, but as in the case of Graves' disease, arteriosclerosis, neurasthenia, etc., is improved by rest, diversion and dietetic control, one might expect that as the depression of the activity of one or more of the kinetic organs has proved beneficial in other kinetic diseases, so surgical measures might be of avail in the treatment of diabetes also.

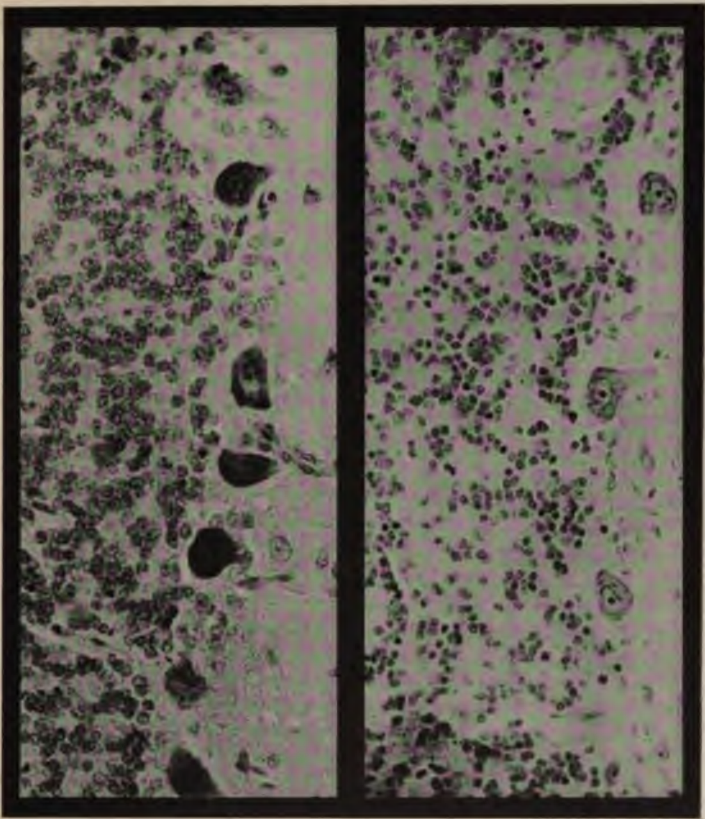
CHAPTER IX

ANOCIATION[1]

In the prevention of surgical shock by *anociation* we have the most convincing test of the practical application of the kinetic theory.[2] In surgical shock the kinetic system is driven to the point of exhaustion by an acute overwhelming activation leading to acute acidosis, the result either of physical injury alone, or of physical injury in combination with preoperative fear. Since shock differs only in degree from any other activation of the kinetic system by physical or chemical stimuli, the prevention of shock must depend upon the possibility of preventing or diminishing the number and intensity of the stimuli which enter the brain by way of either contact or distance ceptors. (Figs. 54, 55, 56.) Such an isolation of the brain is secured in *anociation* (*absence of harmful association*) by dulling preoperative sensibility to all psychic impressions by personal management and, if required, by a preoperative administration of sedatives; by general inhalation anesthesia, which blocks the distance ceptors; and by blocking the afferent nerve paths in the field of operation by means of local anesthesia.

[1] Hereafter the term *anociation* will be substituted for the more cumbersome expression — *anoci association.*

[2] I wish to state here that the statement made by certain writers that I have ever proposed an *inclusive* vaso-motor theory of shock is erroneous.



A. Section of normal cerebellum of dog.

B. Section of cerebellum of dog after surgical trauma.

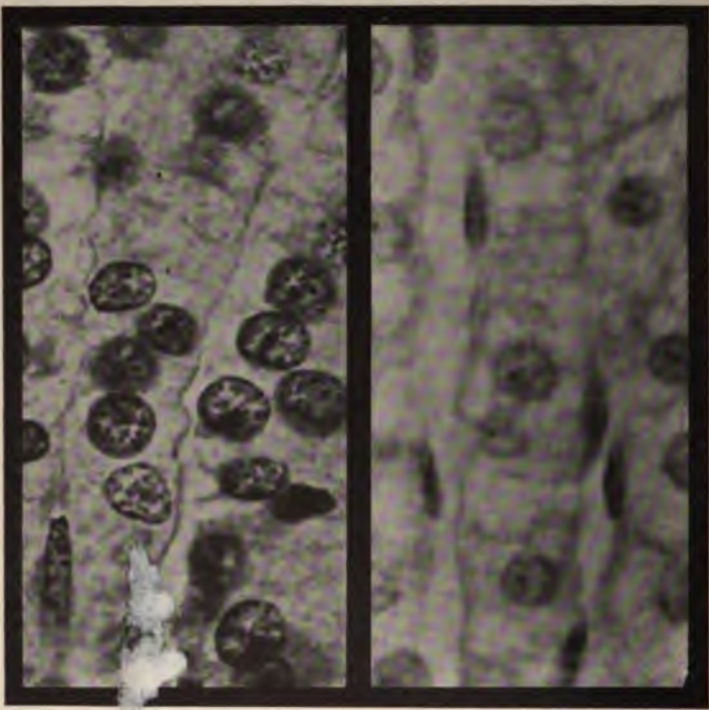
FIG. 54. — EFFECT OF SURGICAL TRAUMA ON THE BRAIN-CELLS OF A DOG.

Compare the hypochromatic appearance of the Purkinje cells in B with the deeply colored, intact cells in A.

(From photomicrographs, × 310.)

Since protection of the patient against fear-producing stimuli before the operation depends largely upon the details of his reception at the hospital, no less than upon his reception in the surgeon's own office, and upon

his preparation for operation, the intelligent coöperation and understanding of every member of the surgical and hospital staff is indispensable to a realization of a perfected *anociation*.

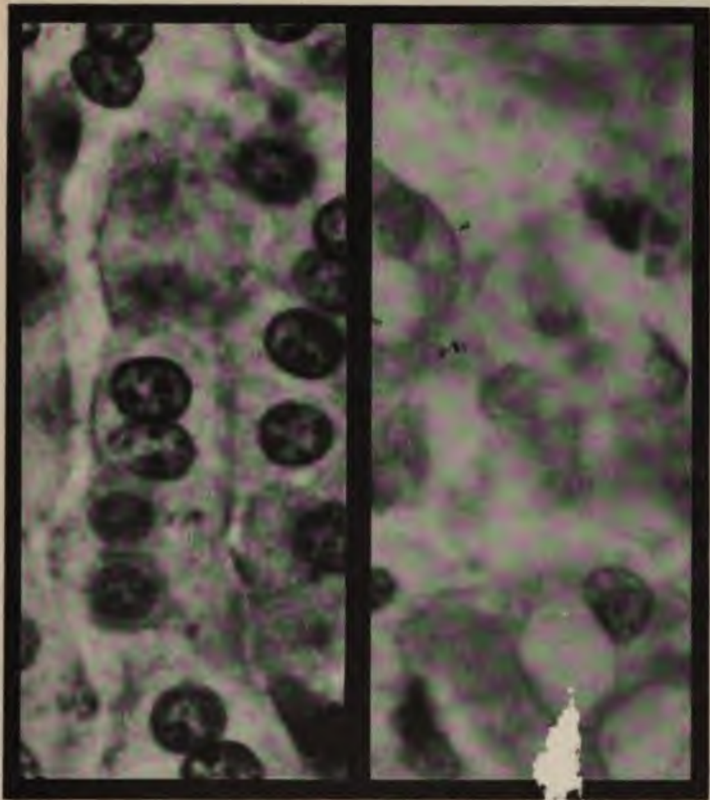


A. Section of normal adrenal of dog.

B. Section of adrenal of dog after surgical trauma.

FIG. 55. — EFFECT OF SURGICAL TRAUMA ON THE ADRENALS OF A DOG. Compare A and B, noting the marked signs of disintegration in B. (From photomicrographs, × 1640.)

If the natural fear of the approaching ordeal, which is felt by every normal individual, be augmented by tactless words in the surgeon's consulting room, by an



A. Section of normal liver of dog.

Section of liver og after surgical tra a.

FIG. 56. — EFFECT OF SURGICAL TRAUMA ON THE LIVER OF A DOG.

Note the vacuolated spaces, the disappearance of nuclei a general disintegration of cells in B.

(From photomicrographs, × 1640.)

ungracious reception at the hospital, by inconsiderate treatment on the part of interne, nurse or orderly, by the sound of clanking instruments or by the rough or forced administration of an anesthetic, then the re-

sistance of the patient, already lowered by his diseased condition, will be still further lowered. No matter how perfect and non-shocking the actual operative technique itself may be, the outcome will be prejudiced by these early adverse factors. (Figs. 57, 58.)

If, however, the preoperative environment of the patient be free from all but the most beneficent suggestions; if his nerves be calmed and his consciousness dulled by the preoperative administration of a sedative;

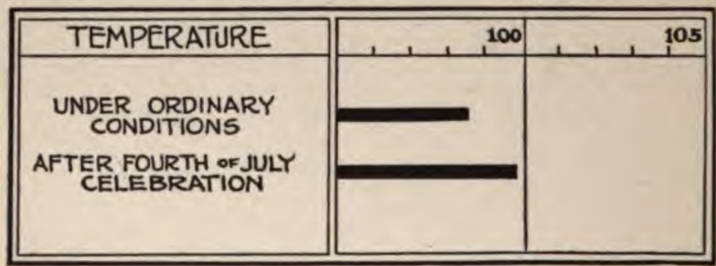


Fig. 57. — Chart Showing Effect of Emotional Excitement on the Temperature.

As a result of a Fourth of July celebration, the children in a ward at Lakeside Hospital showed an average increase in temperature of 1½ degrees F.

if a non-suffocating, odorless inhalation anesthetic be employed; if, during the course of the operation, every division of sensitive tissue, be preceded by the injection of a local anesthetic to cut off from the brain all injurious afferent impulses; and if this be followed by the injection of a second local anesthetic to protect the patient against the painful period of postoperative adjustment; and if gentle manipulation and sharp dissection be used, — if all these measures be employed, the patient will be protected against all damaging factors except those inherent in the diseased or injured condition from which he is seeking relief.

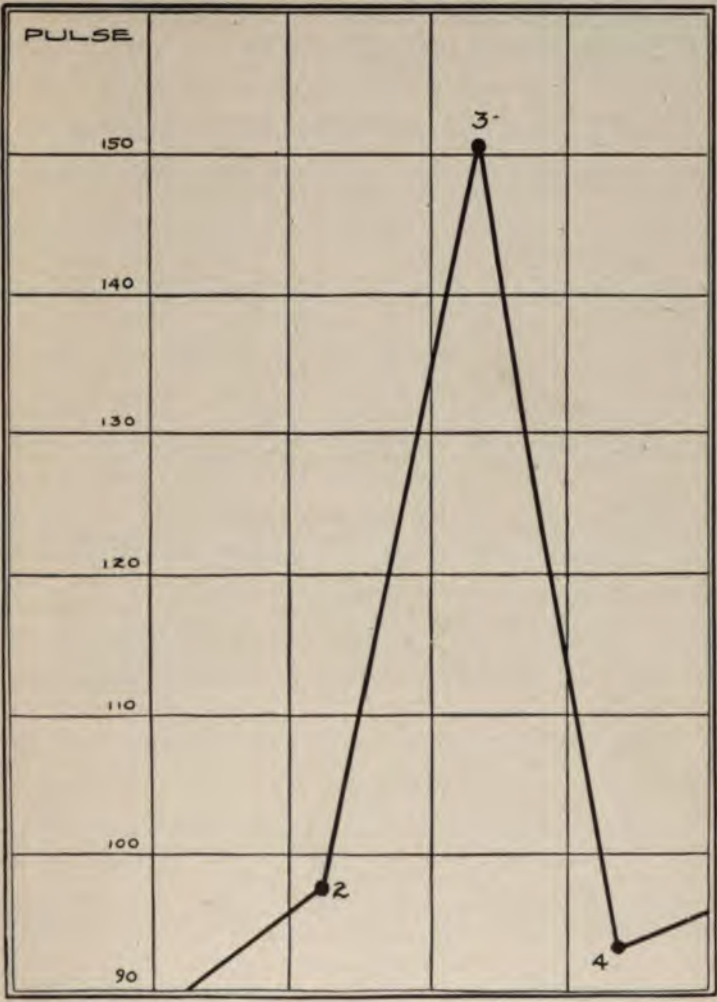
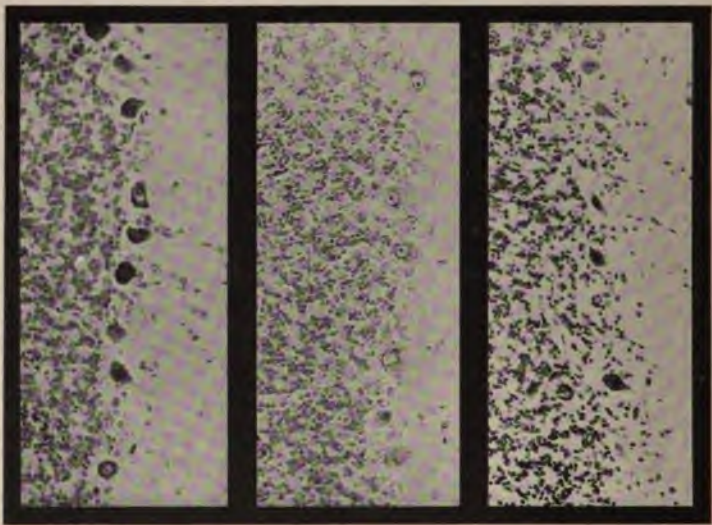


Fig. 58. — Charts Showing Effect of Fear upon the Pulse.

The patient, a foreigner, was brought to the operating room from the accident ward, pulse and temperature normal. When he found himself in the operating room he was greatly disturbed. It was impossible to make him understand that his leg was not to be amputated, but only a plaster cast applied. Under the stimulus of fear his pulse rose to 150, and he soon developed a temperature of 101.2 degrees.

To secure complete freedom from noxious physical and psychic stimuli throughout the whole course of the operation, no one anesthetic is entirely adequate, any more than one set of rules of conduct is applicable to



A.	B.	C.
Section of normal cerebellum of dog.	Section of cerebellum of dog after continuous administration of ether for four hours.	Section of cerebellum of dog after the continuous administration of nitrous oxid for four hours.

Fig. 59. — Comparative Effects of Ether and of Nitrous Oxid on the Brain-cells of Dogs.

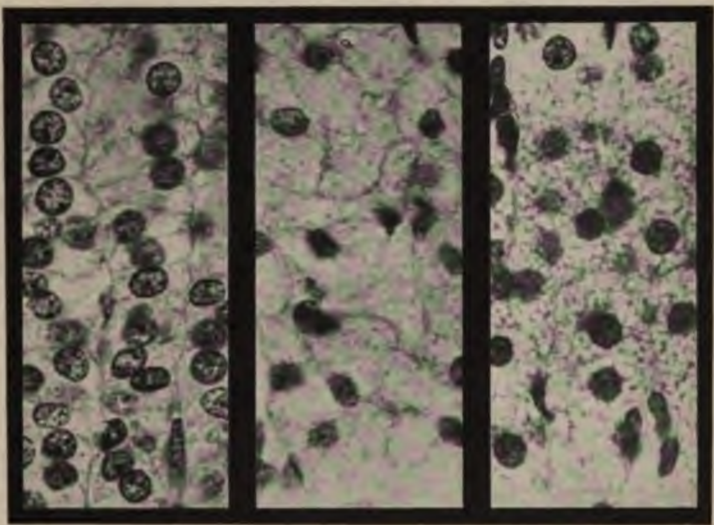
Compare the hypochromatic and disorganized appearance of the Purkinje cells in B with the hyperchromatic Purkinje cells in C.

(From photomicrographs, × 310.)

the handling of every case. An intelligent selection and careful combination of anesthetics, adjusted to the needs of the individual patient, is the rule.

As a general anesthetic in routine cases, nitrous oxid-oxygen is preferred to ether, for many reasons. It

is odorless and non-suffocating; a few inhalations are sufficient to induce unconsciousness; it is less likely to produce nausea than is ether; and laboratory experiments and clinical experience have shown that by the



A. Section of normal adrenal of dog.

B. Section of adrenal of dog after continuous administration of ether for four hours.

C. Section of adrenal of dog after continuous administration of nitrous oxid for four hours.

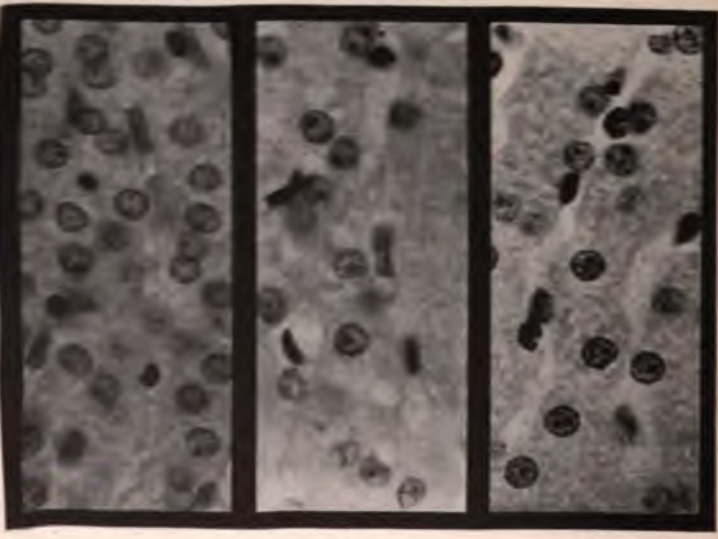
FIG. 60. — COMPARATIVE EFFECTS OF ETHER AND OF NITROUS OXID ON THE ADRENALS OF DOGS.

Note the disappearance of cytoplasm and of some nuclei and the irregular shapes of other nuclei in B as compared with the general conservation of cytoplasm and the well-shaped abundant nuclei in C.

(From photomicrographs, × 1640.)

use of nitrous oxid the organs of the kinetic system are actually to a large extent protected against exhaustion from the traumatic impulses of the operation. (Figs. 59, 60, 61.) Ether, however skillfully administered, induces a period of psychic stress in the earlier stages of

its administration; it immediately impairs the immunity of the patient, since it anesthetizes the phagocytes as well as the patient, and leaves the organism in the position of a citadel threatened by



A. Section of the normal liver of a dog.

B. Section of liver of a dog after the continuous administration of ether for four hours.

C. Section of liver of a dog after the continuous administration of nitrous oxid for four hours.

FIG. 61. — COMPARATIVE EFFECTS OF ETHER AND OF NITROUS OXID ON THE LIVERS OF DOGS.

Although the conservative effect of nitrous oxid is not as evident in the liver as in the adrenals or the cerebellum, yet here also the disappearance of cell substance and of nuclei is much more marked in B than in C.

(From photomicrographs, × 1640.)

attack while its defenders lie drunk in the trenches; it also extends the coagulation time of the blood and makes the danger from hemorrhage more certain. Being a fat solvent, ether dissolves many of the lipoids in the brain, the renal epithelium, the liver and else-

where, thus increasing the amount of waste products to be eliminated, laying a heavier task upon the kidneys, and incidentally increasing the liability to pneumonia, embolism and nephritis. In addition, prolonged etherization causes striking histologic changes in the brain, the adrenals and the liver.

In the choice of the anesthetic, however, it should be emphasized that *the patient is the first consideration,* not the prejudice of the surgeon for a certain method. If nitrous oxid-oxygen does not fully anesthetize the patient, as may happen in some cases and frequently happens with inebriates, then sufficient ether to attain the desired end should be added. It should also be borne in mind always that *while nitrous oxid-oxygen is the safest of all anesthetics in the hands of an expert in the technique of its administration, it is perhaps the most unsafe in the hands of the inexperienced and therefore should never be administered except by an anesthetist specially trained in its use.* In over 14,000 administrations of nitrous oxid by the specially trained anesthetists on my staff, there has been no death.

With the increasing efficiency of the hospital organization and the growing knowledge of the wonderful qualities of nitrous oxid, preoperative sedatives are required less and less.

The peace of mind of the patient having been secured by management and, if needed, by sedatives, and unconsciousness induced by inhalation anesthesia, the operation proceeds, each division of nerve-bearing tissue being preceded by the injection of a local anesthetic — novocain in 1–400 solution. The infiltrated parts are subjected immediately to a firm but gentle pressure

with the hand in order that no nerve in the field of operation may be left free to carry an activating impulse to the brain. If the operation be abdominal, first the skin, then the subcutaneous tissue, then the fascia and, finally, the remaining muscle or posterior sheath and the peritoneum are in turn novocainized, subjected to momentary pressure to spread the anesthetic and then divided within the blocked zone. If the blocking has been complete, then, upon opening the abdomen, the intestines will lie within the abdominal cavity, and the abdominal muscles will be completely relaxed. Under these conditions the entire abdomen may be explored without awakening the nociceptor sentinels. If the operative procedure is such that activation is inevitable, ether is added in advance.

In suitable cases in which *no infection is present*, an additional guarantee against postoperative discomfort may be given by an injection of quinin and urea hydrochlorid, in a $\frac{1}{2}$ to $\frac{1}{6}$ per cent solution. This anesthetic is injected *at a distance* from the line of incision. Its effects last for several days so that by its use the patient is protected from noxious impulses from the operative field until the healing process has well begun.

Results of Anociation

The result of a systematic employment of *anociation* in all cases operated by me in Lakeside Hospital has been to decrease the mortality rate to less than one third the mortality rate before the method of anociation was employed. Unless all facts are known,

however, mere mortality statistics may be of little value to one who contemplates the fact that even a mediocre operator, who possesses the liberty and the judgment to operate only upon those cases which present the required amount of strength to endure his technique and his hospital organization, can show as low a mortality rate as the most expert operator who is supported by the best trained staff but dealing with graver risks. A better clue to the comparative value of methods is to be found in a study of *postoperative morbidity records*. Here *anociation* has assuredly proved its superiority. In comparison with the past records of patients operated under the same general conditions of hospital organization and mechanical technique, but without the protection of *anociation*, the records of the *anoci-protected* cases show a striking diminution in the long train of distressing conditions which are the usual *sequelæ* to operations under ether anesthesia. Shock, gas pain, nausea and vomiting, backache, aseptic wound fever, pneumonia, nephritis, painful scar, neurasthenia and hyperthyroidism are all diminished or wholly prevented by operation under *anociation*.

In the diminution of each one of these common *sequelæ* to surgical operations, there is to be found a significant corroboration of the kinetic theory.

The Kinetic Theory of Peritonitis and Postoperative Gas Pain

The occurrence and prevention of postoperative gas pain may be explained on a biologic basis in the following manner: Prior to the era of aseptic surgery, it may be believed that most if not all abdominal wounds

became infected. Had this state of affairs continued long enough, then, by the law of natural selection, some protective mechanism against infection would have been evolved within the abdomen. The peritoneum possesses such a mechanism, and we believe that the phenomena of gas pain and of peritonitis are parts of a self-defensive reaction. Since infection is most readily spread and increased by movement, immobilization of the abdominal muscles in the infected region is a prime requirement in overcoming any abdominal infection. Within the abdomen, immobilization is secured (1) by the inhibition of the intestines; (2) by the distension of the intestines; (3) by the rigid and persistent contraction of the abdominal muscles; and (4) by the exudation of a sticky, gluelike fluid. The infected point is thus fixed by paralysis; by distension; by *rigidity of the abdominal wall;* and by gluing.

On account of the intestinal inhibition, digestion and absorption cease, and anorexia and vomiting follow, as self-protective measures against the dangers of poisonous, broken-down food products. Pain and tenderness play a part by forcing the maintenance of a boxlike rigidity of the abdomen.

As the abdominal walls are rigid, respiratory movements are confined to the thorax; and since the lungs are thus but partially filled, the respiratory rate is increased to compensate for the diminished volume of exchanged gases. The increased H-ion concentration due to increased energy transformation also tends to increase the respiratory rate. The diminished respiratory excursion and consequent partial venous stasis in the lungs predispose to pleurisy and pneumonia.

The loss of water by vomiting, the diminished intake of water and the failure of water absorption cause a rapid shrinkage of the soft parts which is especially noted in the face, while the increased blood supply to the intestines, combined with the diminished intake of water causes a rapid diminution of the pulse volume. The loss of water is followed also by a diminished volume of urine. At the same time metabolism is increased, and as a result the acid by-products and the H-ion concentration of the blood are increased. The increased H-ion concentration of the blood stimulates the respiratory center. The loss of water and the increased H-ion concentration cause thirst. In this picture of the gamut of the phenomena of peritonitis we see that all are logical results of the activity of a local, self-defense mechanism against infection. Every penetration of the peritoneum initiates this protective mechanism whether there is infection or not — hence abdominal operations are usually followed by gas pain.

If that portion of the brain through which this adaptive response is made be kept in ignorance of the incision into the peritoneum by progressive novocain blocking during the operation and by quinin and urea hydrochlorid blocking to prevent nerve impulses from reaching the brain after the operation, there should be — and there is — diminished or no gas pain. But if, on the other hand, a single nerve pathway escape the blocking and communicate with the brain, there is gas pain, as would be expected.

The same principle is illustrated in the effective treatment of peritonitis by large physiologic doses of opium — the Alonzo Clark treatment. This treatment,

by depressing the activity of the brain, keeps within safe bounds the defensive activity of the kinetic system, which if uncontrolled is prone to exceed the limit of safety. Pain and muscular rigidity are prevented. Metabolism is held practically at a standstill, so there is little need of food; peristalsis is inhibited, therefore the intestines are immobile; and phagocytosis has an opportunity to overcome the infection. This treatment does not replace but supplements surgical treatment.

Painful Scar

The phenomenon of painful scar, which in origin is akin to many pathological as well as normal conditions, may be explained by the fundamental principle of nerve action that any strong traumatic or psychic stimulus produces a change in conductivity somewhere in the cerebral arc, the effect of which is to lower the threshold of that arc. Thus, if a man has been held up at the point of a pistol by a highwayman at a certain street corner, for months afterward whenever he passes that corner that circumstance will be vividly recalled, and perhaps the whole train of activity phenomena following upon the incident may be recapitulated. The effect of traumatic stimuli is similar. The arc receiving strong traumatic stimuli suffers a lowered threshold and from that time on mere trifles become adequate stimuli. Familiar examples of this are the sensitiveness of limbs after fractures, and the painful stumps of amputated limbs; the apparent location of the pain being often not in the remaining stump, but in the part amputated. The lesion of a painful scar, therefore, is not at the site of the wound, but in the brain. Now, if an operation

be so performed that no strong traumatic stimulus reaches the brain, either during or after operation, then the threshold to the cerebral arc from the wound will not be lowered, and the scar will yield no abnormal pain.

Postoperative or Posttraumatic Nervousness

A lowered threshold, resulting from some overwhelming stimulus which predisposes the kinetic system to an uncontrollable discharge of energy in response to trifling stimuli, may explain many abnormal conditions, among them postoperative neurasthenia, which is largely prevented by *anociation.* It is an unhappy reflection upon surgery that the general public has come to expect that a state of nervous derangement, which may last from several months to a year or more, is an inevitable sequel to operations.

When, in the night, one is suddenly awakened by the consciousness of an impending peril, the brain threshold is immediately lowered, apparently as an adaptation for the more swift and accurate perception of the danger. Hearing, sight and sense of touch are abnormally acute. A similar state of universally lowered threshold exists after the receipt of a crushing physical injury. In this tense state, minor stimuli produce major effects, and the individual, in common parlance, is "nervous." In an operation under inhalation anesthesia alone, the unconscious brain has been tortured nearly as much as the conscious brain would be under the same amount of injury and the resultant effect upon the brain threshold is the same. It is not strange that from such an ordeal the patient emerges "nervous"

and "exhausted," to endure a long period of lessened efficiency, of weeping at trifles, of being easily fatigued, of inability to "control" the steady uncalled-for outflow of energy which escapes like flood water over a low dam — a state that will continue until the threshold is raised again by the gradual return of the brain to its normal threshold.

Aseptic Wound Fever and Postoperative "Hyperthyroidism"

The production and the prevention of aseptic wound fever are based, as we believe, upon the physical law that any form of energy may be converted into heat, so that the pain stimuli from a wound may cause the production of both heat and motion. Any stimulus which drives the motor mechanism of the body beyond the point of normal expression will cause fever. Anger, athletic contests, fear, physical injuries, all produce a rapid oxidation, increased temperature and increased acid by-products. In operations under general anesthesia, especially, we expect to see some postoperative rise of temperature as the result of the activation of the kinetic system by the physical and psychic activation of the operation. Since, by the use of *anociation*, we are able to minimize postoperative fever, we conclude that, barring infection and the absorption of hemoglobin, fever after operations under general anesthesia alone is the result of increased transformation of energy, due to activation of the kinetic system by trauma and psychic stress. In like manner *anociation* prevents postoperative "hyperthyroidism" by preventing the activating impulses from reaching the brain during

operations on the thyroid in cases of exophthalmic goiter, thus preventing excessive activation with the resultant excessive acid by-products.

Postoperative Pneumonia

Many theories have been advanced to account for the more frequent occurrence of pneumonia after operations in the upper abdomen, than after operations in the lower abdomen, on the back or on the extremities. That pneumonia is not due to ether alone is proved by its occurrence after operations under local anesthesia. That it is not due to infection alone is shown by the fact that it occurs as frequently in connection with uninfected as with infected wounds. That it is not due to emboli or thrombosis alone is evident from the fact that superficial wounds are rarely followed by pneumonia.

The clue to the real cause is found in a comparison of the postoperative behavior of patients operated upon under *anociation* with those operated upon without that protection. After the *nocuous* operation the wound is tender. As the upper abdominal muscles have specially important respiratory functions, in each respiratory movement these powerful muscles pull on the stitches which hold together the divided wall. The exquisite pain produced by this respiratory pull causes the inhibition of the muscular contractions on the side of the incision, or on both sides if the wound be median. As a result, the excursion of the lower chest wall is diminished, so that the lower lobes of the lungs cannot be filled completely. That a lessened exchange of air in the lower lobes predisposes to pneumonia is suggested

by the frequent occurrence of pneumonia in cases of localized pleurisy, in which pain causes an inhibition of free excursion in the part of the chest which is involved. The resultant pneumonia usually occurs in that portion of the lungs whose free action is inhibited. After gall bladder operations, pneumonia begins usually not in the left but in the right lobe, whereas were the pneumonia embolic in its origin, the lobes would probably fare alike.

The diminution in the number of cases of postoperative pneumonia since the adoption of the technique of *anociation* is final proof of this theory as to its cause. Because of the lack of local tenderness in the field of operation produced by the technique of the operation itself, and by the postoperative nerve blocking with quinin and urea hydrochlorid, there is diminished or no inhibition of the respiratory excursions. This also, without doubt, explains the reduced mortality of operations for umbilical hernia performed with the transverse incision (Mayo).

CHAPTER X

CERTAIN PHASES OF THE RELATION BETWEEN THE KINETIC SYSTEM AND GROWTH, PROCREATION AND CHEMICAL PURITY

In taking possession of the final common path in the brain, stimuli of the external environment, as has been stated, observe a definite order of precedence, depending upon the phylogenetic and ontogenetic meaning of each stimulus to the particular organism in question. In general, it may be said that self-preservation stimuli take precedence over species-preservation stimuli. We postulate that the same order of precedence may be observed in responses to the chemical and physical stimuli of the internal environment of the body.

The stimuli to growth and reproduction, the stimuli of pregnancy, the stimuli to maintenance of the chemical purity of the body, are constantly struggling within the body for the available supply of transformable energy; and the nature of the stimulus gaining possession of the final common path determines many conditions of health and disease in the organism. Sometimes the stimuli of the external environment compete with the stimuli of the internal environment — as when the integration of the body in response to the stimulus of fear interferes with the normal action of the stimuli in response to which nutrition is accomplished — and the sum total of health or disease is the net

result of the balance struck between these competing stimuli of the two environments.

The kinetic system, which is strongly driven by the self-preservative stimuli of starvation, of acute or chronic infection, of physical injury or of overwork; or which is crippled by the deficient functional activity of the brain, thyroid, liver or adrenals, will have a lessened power to respond to the less urgent and more easily deferred stimuli to growth and reproduction. It is known that children grow slowly who suffer from acute and chronic infections, such as oral sepsis, tonsillitis, adenoids, middle ear infection, caries of the bone and indigestion; from impure, improper or insufficient food; from overcrowding, poor ventilation, overwork, cruelty and pain; from deficient functional activity of the thyroid, hypophysis, liver, brain or heart. It is also known that after the removal of these burdens or deficiencies, and the reëstablishment of normal internal and external environments, growth is rapid. This is evidenced by the result of feeding thyroid extract to myxœdematous children; by the rapid growth after the cure of chronic appendicitis, hip joint disease, tonsillitis, adenoids and chronic mastoiditis; after the substitution of happiness and content for homesickness; and of good hygiene for bad hygiene. Interference with growth is in direct proportion to the reduction in efficiency of the kinetic system. It does not matter whether this reduction is the result of a decreased efficiency of some one link in the system, or of an increased call upon the stored energy for response to contact ceptor, distance ceptor or chemical stimuli, so that less energy is left for other demands.

An impairment of the efficiency of the kinetic system by an impairment of the function of one organ in the system is equivalent to an impairment in efficiency through excessive driving of this system — by worry, fear, pain, infection, overwork or by insufficient food. The increased rate of growth in a myxœdematous patient resulting from thyroid feeding is equal to that effected by removing chronically infected tonsils and adenoids, by providing pure milk and good hygiene for the underfed and neglected child or by stopping overwork, pain and worry.

Conversion of Energy for Reproduction

The causes which prevent the transformation of energy by the kinetic system for growth also prevent the transformation of energy for reproduction. The same internal and external stimuli which make an excessive demand upon the kinetic system for self-preservative reactions (diminishing or inhibiting the response to growth stimuli), when present in the growing or adult organism, may prevent or retard the development of secondary sexual characteristics, sexual desire, conception and pregnancy.

It is known that when the thyroid or adrenals are deficient, the development of secondary sexual characteristics is retarded. The development of secondary sexual characteristics may be arrested by excision of the sex glands, and may be delayed by acute or chronic infection, by emotional strain, by auto-intoxication, by pyorrhea alveolaris and by defective hygiene.

It is probable that secondary sexual characteristics and normal sexual function are in part the result of

the action of the internal secretions of the ovaries or testicles upon the kinetic system, by which is produced the kinetic activity required to build up the organs and to create the sex function. Therefore, wherever there is a defect in a link of the kinetic system or absence of efficiency in the ovaries or testicles, there will be a correspondingly diminished expression of sex phenomena.

Such a conception of the development of the function of reproduction might explain why wild animals, as a rule, do not procreate in captivity. Food may be abundant, shelter secure, the kinetic system active, but the *fear integration* excludes the procreation stimulus and prevents energy from being diverted into normal procreative channels. Animals have been so evolved that their tendency to breed is diminished in the midst of hazardous or hostile environments. In the past, such environments would have led to the destruction of mother and offspring; death would have followed procreation in times of drouth and famine and in a period of great cold with scarcity of food. This phylogenetic fact may explain why at any time, when the general nutrition is low, the poverty of the kinetic system is such that energy cannot be spared for procreation.

Maintenance of the Standard of Chemical Purity in the Body

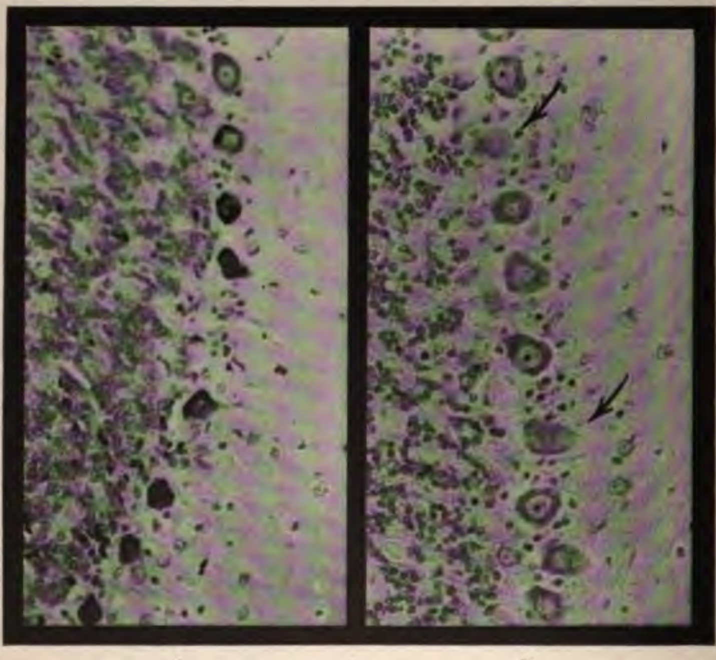
In addition to transforming energy for the adaptive reactions of running, fighting, work, emotion, eliminating foreign proteins, combating infection and furthering growth and procreation, it may be suggested that

the kinetic system transforms energy for the purpose of maintaining the body at an optimum chemical standard and at an optimum bulk. Our evidence for this statement rests upon the fact that most of the metabolic activities which result in the maintenance of the chemical purity of the body are attended by the same phenomena, the same functional and histological changes in the brain, adrenals and liver that are produced by other activations of the kinetic system.

Were not some mechanism in the body adapted to regulate the disposition of food intake, to limit the storage of the digestion products of proteins, carbohydrates and fats, the normal organism in the midst of an abundant food supply would, like sand dunes, continually increase in bulk. That there is such a regulating mechanism, and that this mechanism is the kinetic system, is suggested by the facts about to be presented, which show that intravenous injections of excessive doses of amino acids, of glucose, of alcohol or of fatty acids result in: (1) an increased metabolic activity, *i.e.*, increase in output of calories; (2) an increased activity of the organs of the kinetic system, resulting in functional and histologic changes identical with those produced by running, fighting, emotion or infection (Figs. 62, 63, 64); and (3) a diminished power of the kinetic system to respond to other adequate stimuli.

(1) *Metabolism:* Rubner, Benedict, Lusk, Du Bois and others have shown, by calorimetric methods, that protein injection is followed by an increased production of calories. This is the so-called *mass action*

of proteins. Lusk has shown that the mass action of a protein injection is greater than could be accounted for by the calories of the protein itself. This is explicable on the hypothesis that protein, in excess of the cellular needs, is an adequate stimulus for the kinetic



A. Section of normal cerebellum of cat.

B. Section of cerebellum of cat after injections of leucin.

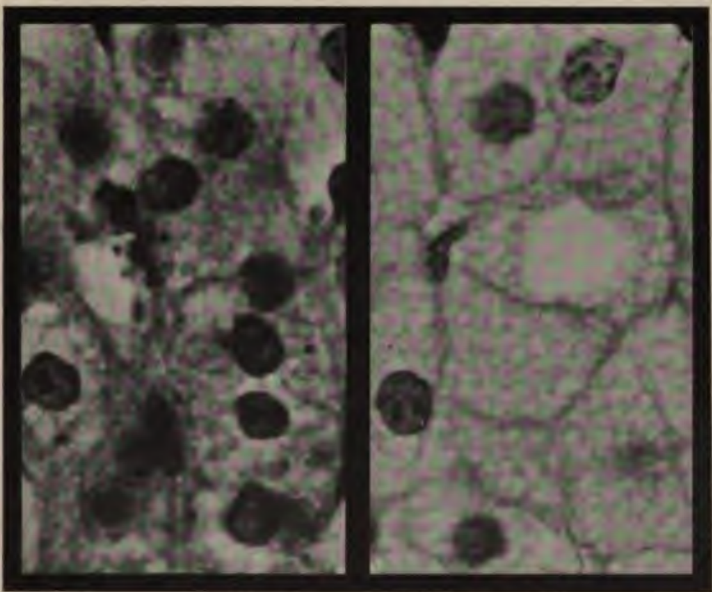
FIG. 62. — EFFECT OF LEUCIN ON THE BRAIN-CELLS OF A CAT.

Note the loss of chromatic material in all and the evidences of disintegration in many of the cells of B.

(From photomicrographs, × 310.)

system. (Figs. 65, 66, 67.) We postulate that it is an adequate stimulus because the kinetic system has been evolved to defend the body against the accumulation

of useless materials of all kinds. Just as the kinetic system utilizes carbohydrates, in responding to bacterial foreign proteins, or in muscular work, so additional carbohydrate energy is used in the work of reducing and eliminating excessive food proteins; and as a con-



A. Section of normal adrenal of cat.

B. Section of adrenal of cat after injections of leucin.

FIG. 63. — EFFECT OF LEUCIN ON THE ADRENALS OF A CAT.

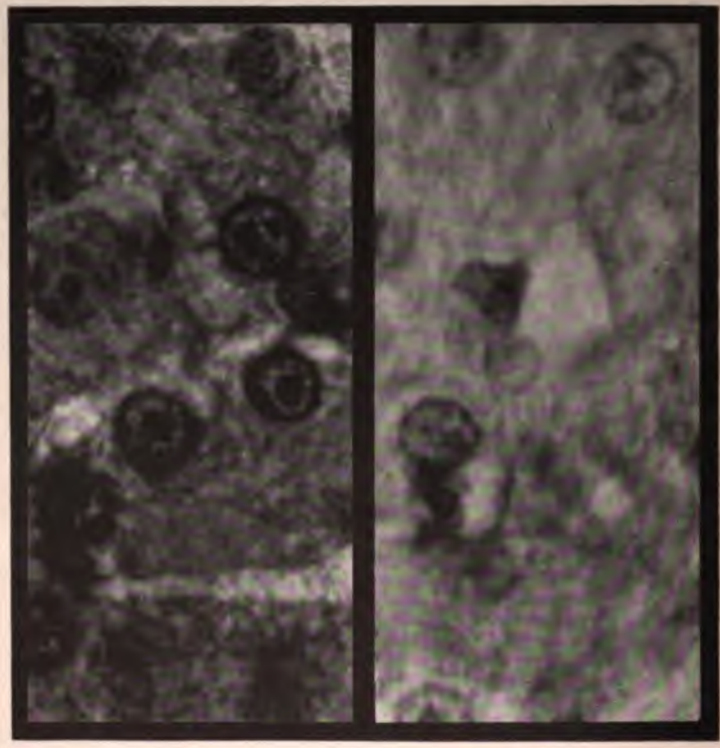
Note the vacuolated space and the disappearance of the nuclei of the cells of B.

(From photomicrographs, × 1640.)

sequence, *the calories produced by protein digestion are greater than the calories derived from the protein itself.*

(2) *Kinetic Activation:* If protein, in excess of the body's needs, acts as an adequate stimulus to the kinetic system, the resultant activation would produce

histologic changes in the brain, adrenals and liver; and functional changes in the thyroid and adrenals identical to the changes produced by muscular work, emotion, infection, etc.



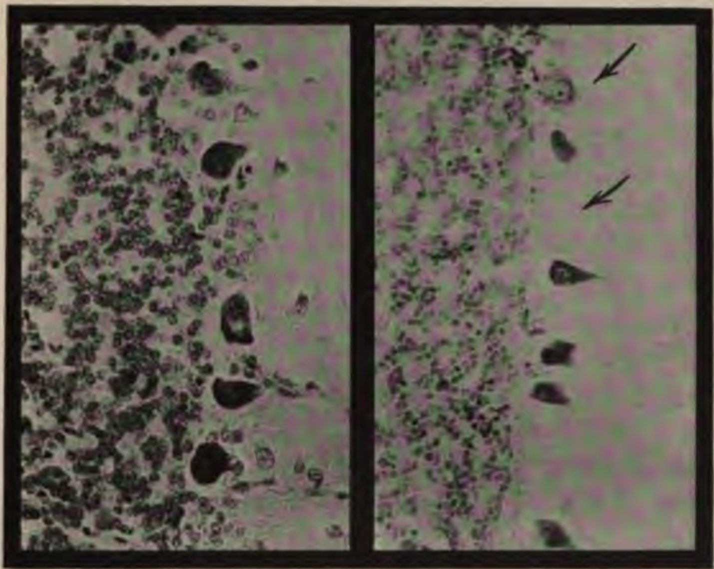
A. Section of normal liver of cat.

B. Section of liver of cat after injections of leucin.

FIG. 64. — EFFECT OF LEUCIN ON THE LIVER OF A CAT.
Note the general disappearance of cytoplasm and of nuclei in B.
(From photomicrographs, × 1640.)

In order to test these points experimentally, we gave to animals intravenous injections of amino acids

(leucin, creatin) and of alcohol, representing the results of protein and carbohydrate digestion. These agents caused an increased output of adrenin and histologic changes in the brain, adrenals and liver, identical with those produced by other kinetic activations, such



A. Section of normal cerebellum of dog.

B. Section of cerebellum of dog after injection of peptone.

FIG. 65. — EFFECT OF PEPTONE (PROTEIN) ON THE BRAIN-CELLS OF A DOG.

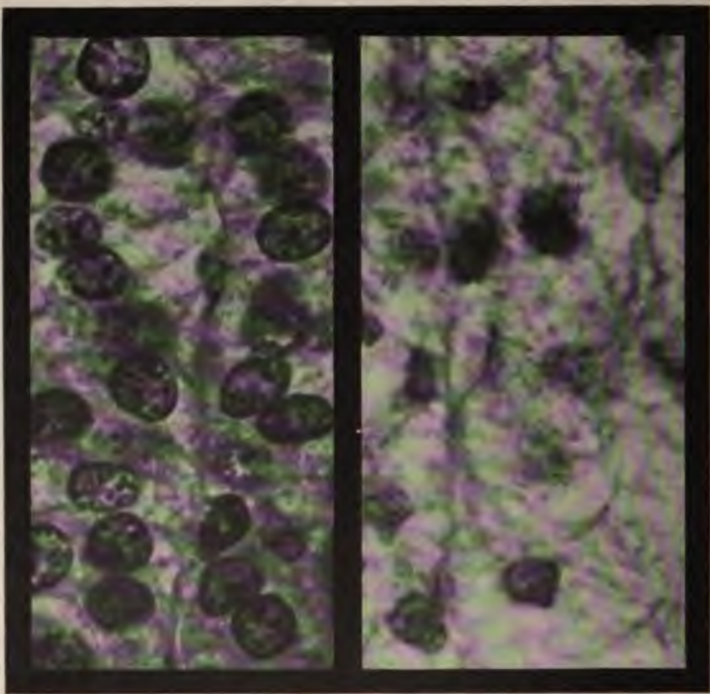
Note the presence of disorganized and fatigued cells in B in contrast to the uniform appearance of cells in A.

(From photomicrographs, × 310.)

as exertion, emotion, infection; clinically it is known that an excessive protein diet aggravates cases of Graves' disease, for which a restricted protein diet is routinely prescribed.

(3) *Diminished Kinetic Efficiency:* If it is the

function of the kinetic system to regulate the amount of food products stored in the body, then, when an excessive amount of food is ingested, the kinetic



A. Section of normal adrenal of dog.

B. Section of adrenal of dog after injection of peptone.

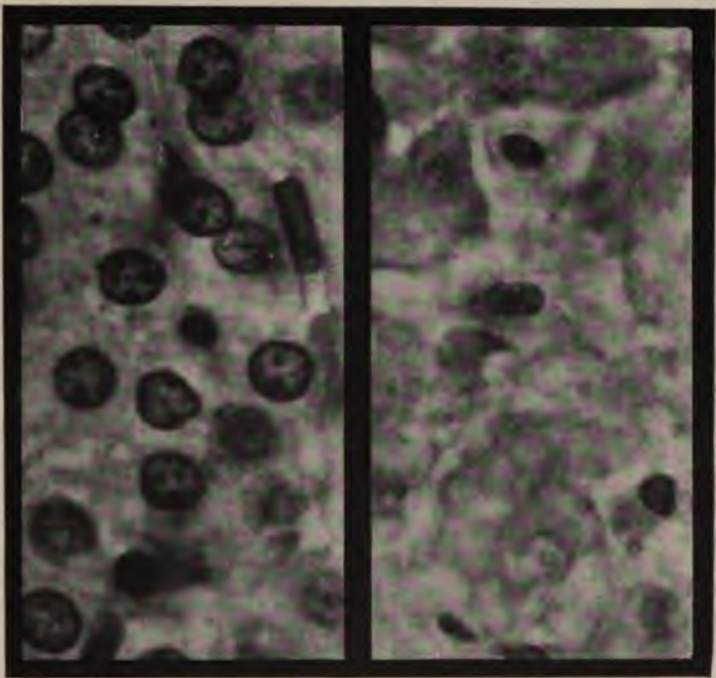
FIG. 66. — EFFECT OF PEPTONE (PROTEIN) ON THE ADRENALS OF A DOG.

Note the vacuolated spaces, disappearance of cytoplasm and the irregularly placed nuclei of the cells of B, as compared with A.

(From photomicrographs, × 1640.)

system, occupied with breaking down and eliminating this excess, will be rendered unable to respond normally to other stimuli, such as stimuli to mental and muscular work, emotion, etc. The general inef-

ficiency of the overfed is patent to every one. It is an interesting fact also, as shown by Du Bois, that protein injection does not produce increased calories



A. Section of normal liver of dog.

B. Section of liver of dog after injection of peptone.

FIG. 67. — EFFECT OF PEPTONE (PROTEIN) ON THE LIVER OF A DOG.

Note the disappearance of cytoplasm, the disappearance of some nuclei and the irregular shapes of others in B.

(From photomicrographs, × 1640.)

in the presence of fever, as would be expected. The reverse would be as improbable as it would be for an engine to blow off steam while it is struggling with a heavy overload.

Since excessive protein diet causes the same kinetic activation as overwork, worry or infection, we can understand why it can also precipitate the same kinetic diseases; why, also, though it may not be the real cause of any given disease, it nevertheless may be an injurious aggravating factor; and why limiting the protein diet of one suffering from a disease of the kinetic system may be as beneficial as rest, freedom from worry or getting rid of an infection. We can understand how cardiovascular and cardiorenal disease may be produced by excessive food; and how they may be aggravated by excessive muscular work, and improved by muscular repose; how nephritis may be augmented by excessive protein diet or improved by a rigidly limited diet.

By this conception we link "metabolism" with other adaptive reactions which involve the kinetic system and are governed by the internal and external environment. In other words, metabolism is not the *cause* but the *result* of internal or external environmental stimulation of the kinetic system. When the kinetic system is activated, metabolism results; when the kinetic system is quiescent, metabolism is quiescent; when a link of the kinetic system is impaired, metabolism is impeded. When one link of the kinetic system is completely broken, metabolism — the transformation of energy — ceases. Metabolism depends upon the unity and integrity of the kinetic system as much as the complete action of an automobile depends upon the integrity of the essential parts of its motor. In fact the kinetic system *is* the motor of the body, the driving power — and no less the *driven*

power — as a result of whose action *metabolism* is produced.

Pregnancy and Eclampsia

Although, through the action of the kinetic system, the species preserves a relative purity of its chemical composition, observation shows that this standard is not always identical. The development of serologic knowledge has disclosed certain variations among normal individuals. Hektoen showed that the serum of particular groups of individuals contained isoglutinins for certain other groups, and no isoglutinins for still other groups. The source of this difference has not yet been determined. Not only is the lack of absolute chemical homogeneity among individuals shown by serologic tests, but it is also shown by the more rigid test of the transference of living parts of one animal or man to another. These observations have been made on a large scale in the direct transfusion of blood, in skin grafting and in the transplantation of organs.

In blood transfusion hemolysis of the transferred blood might be easily understood when the recipient is abnormal, as, for instance, where there is pernicious anemia; but there is also a slight hemolysis of transferred blood in some apparently normal individuals. This would indicate a difference in the chemical nature of normal individuals. As to skin grafting, I have observed that, in cancer, skin grafts from the patient himself are far more successful than skin grafts from another individual. Even in the absence of disease, skin grafts from another part of the same individual grow better than grafts from another individual. Carrel

has shown conclusively that, in some instances, organs transplanted from the body of one animal to the body of another of the same species may undergo histologic changes. Most transplanted kidneys are broken down in time. Lexor's brilliant surgical feat of transplanting entire knee joints from one human being to another showed later that the transplant gradually disappeared and was replaced by a new structure identical in form and bulk with the transplant, but actually the result of cell multiplication by the host organism. Thus we have experimental and clinical evidence that normal individuals of the same species may possess slight chemical differences.

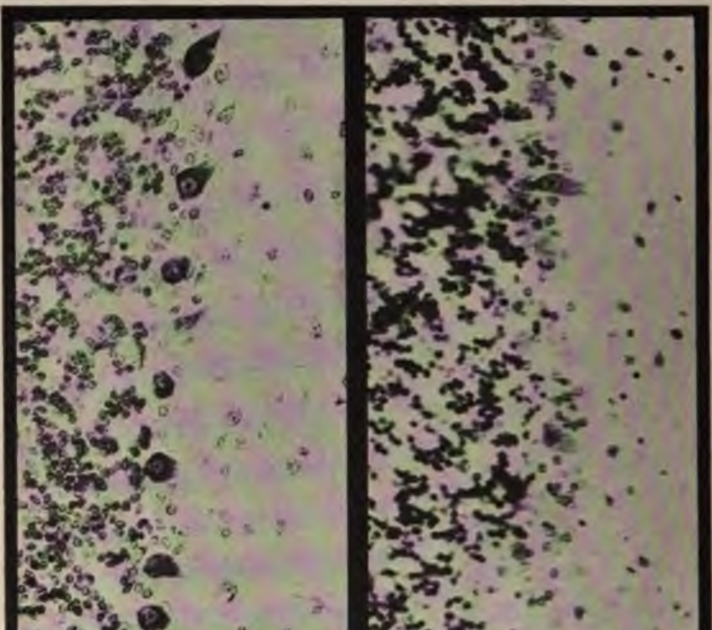
The beginning of the process of procreation is the transplantation of a unit of tissue from one individual of a species to another individual of the same species. Species are probably only exaggerated varieties; and varieties are exaggerations of individual differences. The reason why different species do not cross is doubtless because the chemical reaction of the female kills the spermatozoön, which is a foreign protein. The same reason doubtless explains why varieties cross less well than individuals of the same species. And one may assume that two normal individuals who produce no offspring, but who, when they separate and remate, are fertile, are infertile in the first instance because of chemical incompatability.

The spermatozoön presumably brings with it the chemical characteristic of the male. Hence, in the growth and development of the placenta and fetus there should be a slight chemical difference between the mother and the fetus, which would increase dur-

ing the period of fetal growth. The female therefore would have an increasing chemical difference to overcome. We have seen that the standard of chemical purity of the body is maintained through the action of the *kinetic system*. When there is a chemical difference between the growing fetus and placenta, therefore, the kinetic system of the mother would be activated exactly as when any other foreign protein is present in her body. An added increase in the work of the kinetic system would be imposed. Also, the increase in metabolism required for the growth and activity of the fetus would give an increased production of acid by-products as a result of the increased energy transformation. That the needs of the fetus are considerable is shown by the fact that during pregnancy the total food intake of the mother is greatly increased. As a result of this increased intake of food, the elaboration of material for the growth of the fetus, and the added burden of overcoming the difference in chemical standards, the kinetic system of the pregnant mother should and does exhibit greatly increased activity, as is shown by the following evidence:

Brain: In the pregnant state there is progressive loss of muscular power, mental efficiency and resistance to infection. Memory, reason and endurance suffer just as they do in infection or in auto-intoxication. More direct evidence of the effect of pregnancy on the brain was found by examining the brain-cells of pregnant rabbits and cats. In our histologic studies of normal pregnancy we found evidence of brain overwork and brain deterioration. The percentage of hypochromatic brain-cells was above normal. In addition

we found that the intravenous injection into the mother (rabbit) of extract of her own placenta produced typical work changes in the organs of the kinetic system. (Fig. 68.) Thus, we have direct physical evidence to



A. Section of normal cerebellum of cat.

B. Section of cerebellum of pregnant cat.

FIG. 68. — EFFECT OF PREGNANCY ON THE BRAIN-CELLS OF A CAT.

The effect of the long activation of pregnancy is well illustrated by the generally disorganized appearance of the Purkinje cells in B.

(From photomicrographs, × 310.)

confirm and support the experiences of everyday life. The reason why there are changes in the brain-cells and why there is evidence of fatigue is because the

brain has been driven to overwork by the requirements of pregnancy.

Adrenals: It is known that the adrenals enlarge in animals in advance of their mating season and that the enlargement persists during pregnancy. Such

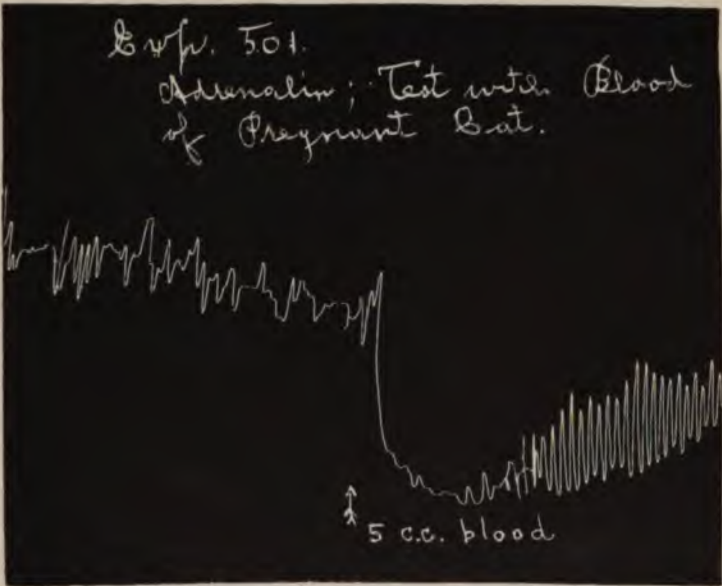


Fig. 69. — Tracing Showing Effect of Pregnancy on the Adrenal Output of a Cat. (Cannon Test.)

That the adrenal glands are activated during pregnancy is demonstrated by the sharp inhibition of the contractions of intestinal muscle when the blood of a pregnant cat is substituted for normal blood.

seasonal enlargement and its persistence during pregnancy indicate an adaptation to the work of pregnancy — a preparation on the part of the adrenals for a useful participation in pregnancy. In addition to this anatomical evidence, we found an increase of adrenin in the blood of a pregnant rabbit. (Fig. 69.) Further-

more, we found that intravenous injection of placental extract caused an increased output of adrenin in the mother rabbit. In addition, we have shown in our laboratory that histologic changes in the adrenals are produced during normal pregnancy in cats and rabbits. This evidence would seem to indicate that during pregnancy the adrenal link in the kinetic system performs more than its normal amount of work.

Thyroid: The thyroid enlarges during the mating season. It enlarges during courting and mating; in most women, the thyroid undergoes some enlargement during pregnancy. This enlargement may disappear at the termination of pregnancy, and the gland return to its normal condition. But in many instances a part of the enlargement persists, and is increased with each succeeding pregnancy, resulting finally in a large goiter.

That this enlargement is a work phenomenon is evidenced by the facts that in pregnancy the thyroid not only is enlarged but becomes more vascular and that two goiters excised during pregnancy from patients having no symptoms of Graves' disease and no infection, showed typical glandular hyperplasia. No other cases of such typical glandular hyperplasia have been found, excepting in patients whose kinetic systems were known to be activated, as, for instance, in Graves' disease, chronic pyogenic infection or tuberculosis. There is additional evidence, moreover, that the thyroid is hyperactivated in pregnancy. The pregnant woman has the symptoms of mild Graves' disease, excessive thyroid feeding or excessive administration of iodin, namely: excitability, tremors, exhaustion, sleeplessness, increased metabolism, increased heart beat,

increased respiration, sweating. She is easily fatigued. Finally, negative proof is found in the fact that if iodin or thyroid extract in small doses be given during pregnancy, the thyroid will enlarge little if at all. The function of the thyroid is to metabolize iodin, that is, to make iodin available for use in the body economy. Hence, when there is hyperplasia of the thyroid, we assume that the gland is responding to an increased call for iodin. This evidence shows that the thyroid, like the brain and adrenals, is activated during pregnancy.

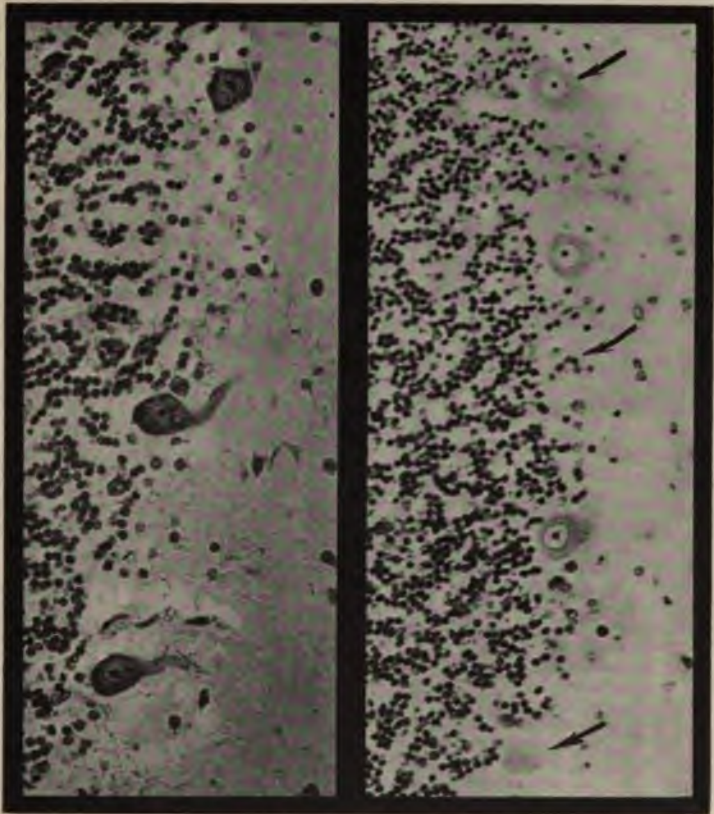
Muscles: Clinical evidence of the participation of the muscles in the activation of pregnancy is found in a distinct loss of muscular power, which may be due to the increased activity of the muscles in maintaining the standard of chemical purity through heat production. The muscles participate largely in heat production, and during pregnancy the body temperature is slightly above normal and further increase of temperature is made with abnormal facility.

Liver: That the work of the liver is increased in pregnancy is shown by urinary findings. If toxemia be present, the decrease in the urea and the increase of ammonia show that the liver is no longer able to perform the entire task of reducing the end products of protein metabolism. In the toxemia of pregnancy the appearance of a high blood-pressure, as in cardiorenal disease, and the increased H-ion concentration of the blood in the stages nearing eclampsia (Michaelis) offer clinical evidence that excessive work is performed by the liver in pregnancy. Further evidence of this fact is seen in the histologic studies of Ewing, which show that massive degeneration of the liver takes place in the

toxemia of pregnancy, and in our own laboratory findings of histologic changes in the livers of cats and rabbits in normal pregnancy. Moreover, Lusk and his co-workers have demonstrated by exact calorimetric methods that there is an increased energy transformation (metabolism) during pregnancy.

According to this reasoning, eclampsia may be regarded as the end result of a failure of the mechanism whose special function is the neutralization of the acid by-products resulting from the increased energy transformation of pregnancy. Ultimately, the liver gives way under the strain and becomes so incapacitated that the acid by-products of metabolism are not completely neutralized and in consequence there occur acidosis, headache, drowsiness, stupor and convulsions. The phenomena of puerperal eclampsia have many points in common with those attending the breakdown of the acid-neutralizing mechanism in Bright's disease, in diabetes and in cirrhosis of the liver. The pathologic phenomena of pregnancy may thus be explained as the result of excessive activation of the kinetic system. (Fig. 70.) The kinetic system takes much of the burden of producing offspring, just as it takes the burden of securing food, of combating enemies, of avoiding danger, of expressing the emotions, of overcoming infections and of maintaining the chemical standard of the body. In the amount of excessive energy transformation it entails, pregnancy may thus be compared to infection, emotion, etc.

As a corollary, we may understand why pregnancy does not occur if there be deficiency of the two great activators of the kinetic system — the thyroid and the



A. Section of normal human cerebellum. (After accidental death.)

B. Section of human cerebellum after death from eclampsia.

FIG. 70. — EFFECT OF ECLAMPSIA ON THE BRAIN-CELLS OF A HUMAN BEING.

Note the general disintegration and loss of chromatic material in the cells indicated by arrows, as compared with the deeply stained, intact cells of A.

(From photomicrographs, × 310.)

adrenals; and conversely why pregnancy in anemic, chlorotic, adynamic women sometimes transforms them and gives them added weight and added energy.

Though this explanation is wholly theoretical, it is conceivable that the vomiting of pregnancy may be due to the same cause as vomiting in acute infections or during the absorption of foreign proteins. When the body needs to split up and eliminate a foreign protein, the kinetic system will more readily accomplish this work if no more added food be taken, thus avoiding the additional work of breaking down and eliminating the amino acids derived from normal food. Thus, the foreign proteins of the chemical invasion incident to procreation (the fetus and placenta) may exert the same influence as that exerted by the chemical invasion in the form of bacteria. If the foreign proteins in bacteria can cause active vomiting, why may not the growing massive "foreign proteins" of pregnancy? We have some evidence to support such a view in the fact that the moment the uterus is emptied, the vomiting ceases; or if the fetus dies, the vomiting ceases. It has been offered as an explanation that the vomiting is reflex and is due to a false position of the uterus or to the mechanical expansion of the uterus by the fetus. Against this, it may be pointed out that mechanical pressure, false position, tension or surgical dilatation of the normal uterus cause no nausea; and also that, as already stated, whatever the false position of the uterus, death or expulsion of the fetus at once ends vomiting.

Since man is a transformer of energy, his unborn offspring are also transformers of energy. If after his birth man's further growth and maturity can occur only through the activity of his kinetic system, we have no reason to doubt that the growth in the uterus

is made possible only through the work of the kinetic system of the mother, aided, as the fetus develops, by the kinetic system of the child. This much is certain, that the growth of the fetus in the uterus is at a more rapid rate than its growth after birth.

A prematurely born infant, — one delivered at six months, — which is kept at as even a temperature in an incubator as in the uterus, does not show a rate of growth equal to that of the fetus within the uterus. The infant is now depending upon its own kinetic system alone. That the kinetic systems of mother and offspring work together is shown by the fact that if the mother has a deficient thyroid gland, the new-born babe may have a goiter, showing that the thyroid of the fetus was called upon to supply the lack of thyroid secretion, although whether this call was made by the organism of the mother or of the fetus, or of both, is not known. A possible evidence of the excessive demand upon or of the deficiency of the adrenal secretion is seen in the characteristic brownish discoloration of the skin of pregnant women. These discolorations are analogous to those of Addison's disease and appear with pregnancy and disappear after delivery.

At term, the phenomena of labor present interesting examples of adaptive reactions. The preliminary pain compels attention — rest. The entire process, from the warning pain to the muscular contractions and muscular relaxations of delivery, is all an adaptation to facilitate the birth. Birth opens an enormous bleeding area. Vast blood vessels are rent asunder. Large raw areas of uterine tissue are exposed to infec-

tion. Yet, in the school of natural selection there have been evolved mechanisms of protection against all these menaces — mechanisms for the arrest of hemorrhage through uterine contractions and through facilitated clotting, and mechanisms in the tissues of the genital tract and genital organs for protection against infection. In its excellent endowment with mechanisms of protection against the hazards incident to its function the genital tract is analogous to the gall bladder and the urinary bladder which are protected against communication with infected territories.

Thus, in the fundamental processes of courtship, conception, pregnancy, birth and the rearing of the young do we find a series of wonderful adaptations by means of which the species effects survival.

CHAPTER XI

A MECHANISTIC INTERPRETATION OF THE ACTION OF CERTAIN DRUGS

No more striking evidence that the organism is a physico-chemical mechanism governed by the laws of physics and of chemistry can be adduced than the reaction of the organism to certain drugs. We shall select therefore from a large amount of data facts concerning certain drugs which offer striking confirmatory evidence in support of our major theme.

In general, according to their effect upon the kinetic system, drugs may be divided into two classes: *first*, those that stimulate the kinetic system to increased activity, and as a consequence produce histologic changes in the brain, the adrenals and the liver; and *second*, those that suspend or depress the activity of the kinetic system, and as a consequence conserve the kinetic organs, as is evidenced after their administration by the lack of histologic changes in the brain, the adrenals and the liver, and in some instances by increased hyperchromatism, indicating that during the quiescent period the stores of energy in the brain, at least, have actually been increased.

Strychnin

Our experiments have shown that the changes in the kinetic organs produced by drugs of the first class

are precisely the same as the cycle of changes produced by the emotions, physical exertion or other forms of kinetic stimulation. For example, according to the dosage, *strychnin* causes intense excitement — convulsions — ending in exhaustion and death; a lesser degree of excitation followed by lassitude; slight stimulation without notable after-results; while the histologic changes in the brain, adrenals and liver — especially marked in the brain — display these physiologic alterations in proportional *hyper*chromatism in the active stages and *hypo*chromatism in the stages of reaction.

Opium

Abundant clinical and experimental evidence exists to show that *opium* blocks or depresses the cerebral link of the kinetic system. Every one knows that deep opium narcotization prevents anger, fear, shock, muscular and mental work, and in addition the clinician knows that opium diminishes fever and controls anaphylactic phenomena. Of most vital significance to our theme, however, is the fact, established by laboratory experimentation, that deep opium narcotization prevents the output of adrenin. (See Fig. 48.) Even in large doses, however, opium does not prevent the action of adrenin injected intravenously. We have shown in previous chapters that adrenin is a powerful activator of the kinetic system, but it may be well in this instance to refer again to the fact that adrenin causes all the phenomena of kinetic activity — with one exception, an increase in adrenal output. Adrenin causes all the phenomena of fever,

of emotion and of physical exertion and even prepares the way for gross muscular activity in that it increases the capacity of the muscles to use glycogen (Cannon); and most significant of all, adrenin facilitates the elimination of the acid by-products of muscular action. *Any agent, therefore, that controls the output of adrenin controls proportionally the conversion of energy into heat and motion.*

If *opium* acts directly on the central battery — the brain — so that its energy cannot be mobilized to drive the various organs of the body, one would infer that through its action on the brain, opium must prevent the histologic changes produced by kinetic stimuli. The truth of this inference is strikingly evidenced by experiments in which rabbits were given large doses of morphin either before or immediately after receiving doses of diphtheria toxin. Histologic examination of the brain, the adrenals and the liver of each of these animals showed that the morphin had almost wholly prevented the histologic changes which previous experiments had shown to be caused by diphtheria toxin alone.

In studying the effect of morphin on the H-ion concentration of the blood, we found that deep narcotization does not change the normal alkalinity of the blood — at least not until the stage of asphyxia in fatal cases; that in a morphinized animal psychic and traumatic stimuli cause neither the clinical nor histologic changes nor the degree of acidosis normally associated with a comparable degree of kinetic stimulation of like type; but that the administration of morphin *after* the H-ion concentration of the blood

had been increased by exertion, by fear, or by inhalation anesthesia delayed the return of the blood to its normal alkalinity. From these observations we infer that morphin interferes with the activity of the mechanism by means of which acidity is overcome and by which the normal alkaline state is maintained. In this fact we find further evidence that oxygen metabolism is as important in acid elimination as in acid production.

These facts from the laboratory and the clinic lead to the conclusion that through its specific action on the brain, opium controls the kinetic system and therefore governs the rate and extent of energy transformation in response to kinetic stimuli whether from the internal or the external environment. If this be so, then opium may be made to serve a beneficial purpose in protecting the kinetic system from exhaustion and death from excessive acute activation. It is known that opium improves certain chronic diseases, in the etiology of which kinetic activation plays an important rôle, such diseases, for example, as cardiovascular disease, Bright's disease, neurasthenia, Graves' disease, etc. What is accomplished by rest for these cases may be temporarily accomplished by opium.

Opium is almost a specific in the prevention of shock and in urgent cases, therefore, the preoperative administration of morphin is an essential part of the complete technique of *anociation*. Since, as we have stated, opium interferes with the neutralization of acidity, it is especially indicated as a preventive of shock, and is contraindicated during inhalation anesthesia.

Not only the shock which results from physical trauma but psychic shock as well may be mitigated by the administration of opium. Before the days of anesthesia heavy doses of laudanum diminished not only the pain but the dread and struggles of the patient to whom the solace of unconsciousness during an operation was denied. During the French Revolution the public executioner gave opium to his victims to diminish their struggles and protests. When under the influence of opium, a cat will not spit at a dog; a rabbit has no fear. Under opium no one is either brave or a coward, but is in a negative state into which psychic stimuli cannot penetrate.

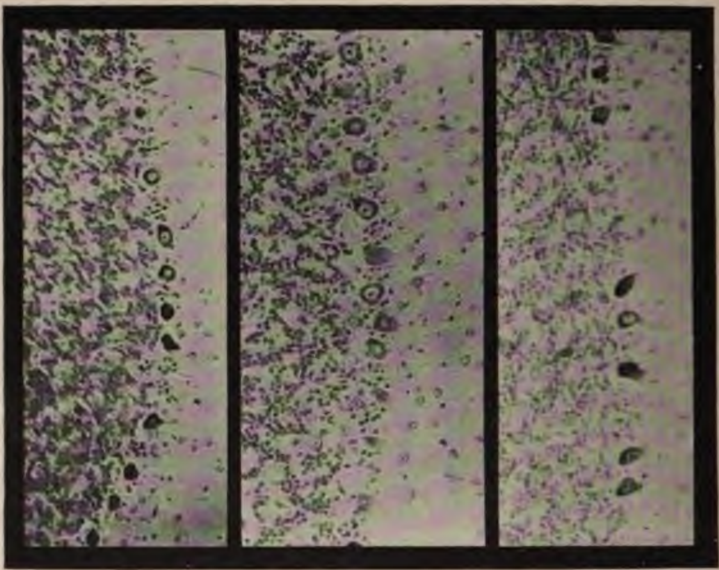
In cases of exophthalmic goiter the administration of opium will minimize or prevent the hyperthyroidism due to psychic or physical trauma. In extreme cases of Graves' disease, however, when the acid-neutralizing organs — the liver and adrenals — are nearly exhausted and a state of acidosis exists, morphin is unsafe, since it will further retard the already failing acid-neutralization.

It is probable that most deaths from acute infection are the result of an activation of the kinetic system to the breaking point. This fatal exhaustion in acute overwhelming cases may therefore be prevented by deep opium narcotization. In the last generation the value of opium in these cases was more generally recognized than at present. By the so-called "Alonzo Clark" method, opium was given in sufficient dosage to overcome abdominal distension and reduce the respiratory rate to eight or ten per minute. In this trancelike state the kinetic system was held almost at a stand-

still, the energy in the body thus being conserved until phagocytosis overcame the infection.

Acids and Alkalies

Laboratory experiments in which an acute acidosis was produced by the injection of various acids —



A. Section of normal cerebellum of cat.

B. Section of cerebellum of cat after injection of acid sodium phosphate.

C. Section of cerebellum of cat after injection of sodium bicarbonate.

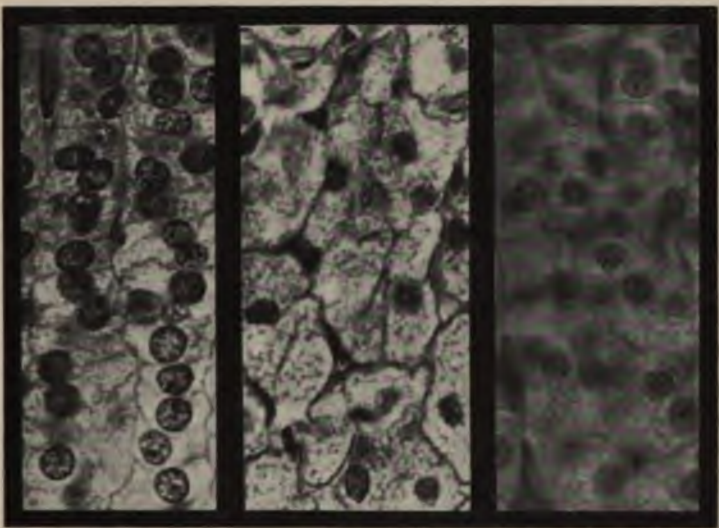
FIG. 71. — THE COMPARATIVE EFFECTS OF AN ACID AND OF AN ALKALI ON THE BRAIN-CELLS OF CATS.

Compare the Purkinje cells in the three sections, noting in C the conserving effect of the alkali as compared with the disorganizing effect of the acid in B.

(From photomicrographs, × 310.)

hydrochloric acid, acid sodium phosphate, etc. — directly into the circulation gave ample evidence in gross phenomena and in histologic changes of the

fact that acids interfere with the activity of the kinetic system. In every case extensive histologic changes were seen in the brain, the adrenals and the liver; and iodin determinations gave evidence of the fact that there was increased thyroid activity also.



A.	B.	C.
Section of normal adrenal of cat.	Section of adrenal of cat after injection of acid sodium phosphate.	Section of adrenal of cat after injection of sodium bicarbonate.

FIG. 72. — THE COMPARATIVE EFFECTS OF AN ACID AND OF AN ALKALI ON THE ADRENALS OF CATS.

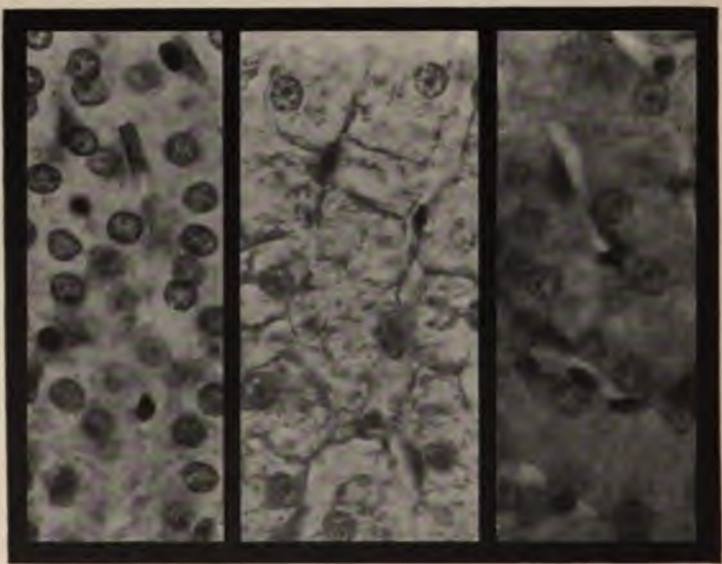
Note the disappearance of cytoplasm in C, and the eccentric and crenated nuclei as compared with the nearly normal appearance of C.

(From photomicrographs, × 1640.)

On the other hand after the administration of an alkali — sodium bicarbonate — histologic studies of the brain, the adrenals and the liver showed a *hyperchromatic* condition corresponding to the *hyperchromatic* condition produced by the administration of morphin

alone, thus showing that alkalies tend to conserve while acids destroy the mechanism of energy transformation. (Figs. 71, 72, 73.)

Clinical evidence of the protective value of alkalis is shown by the value of the administration of sodium



A.	B.	C.
Section of normal liver of cat.	Section of liver of cat after injection of acid sodium phosphate.	Section of liver of cat after injection of sodium bicarbonate.

Fig. 73. — The Comparative Effects of an Acid and of an Alkali on the Livers of Cats.

Note the disappearance of cytoplasm and of nuclei and the vacuolated spaces in B as compared with the conservation of cell substance in C.

(From photomicrographs, × 1640.)

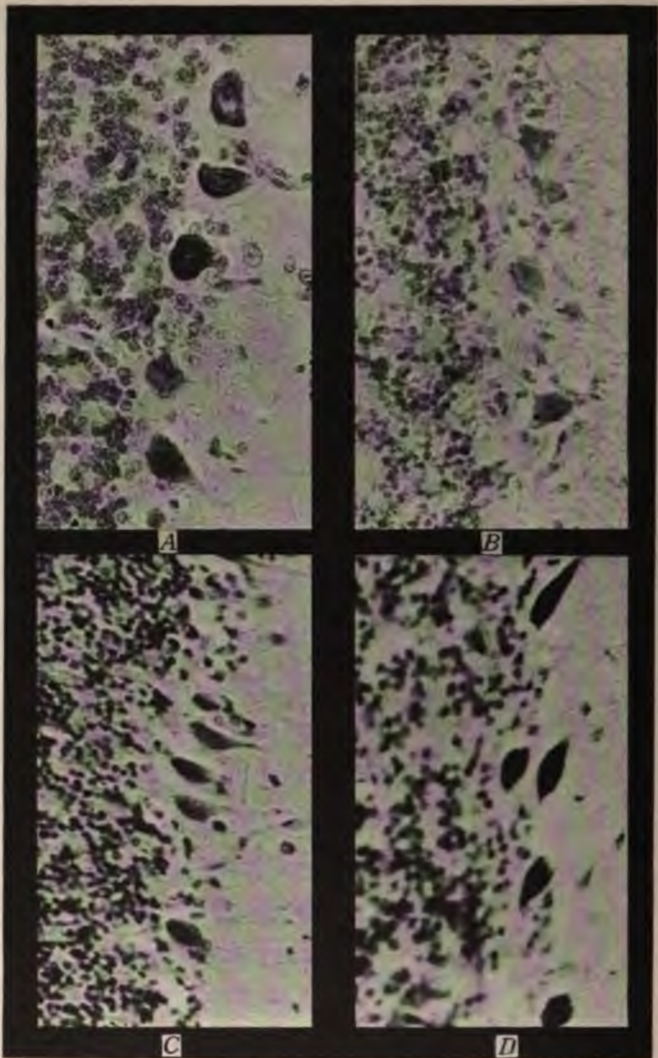
bicarbonate in cases in which acidosis is present or is impending, and by the widespread medical use of the conserving alkalis and the restricted use of the destroying acids. No one recommends acid mineral springs.

Iodin — Adrenin

The effects of these substances, which are the essential constituents of thyroid secretion and of adrenal secretion respectively, and the adaptive reaction of the organic mechanism to each have already been fully discussed. It is sufficient here to repeat that both iodin and adrenin cause increased energy transformation, the one almost instantaneously, the other after a latent period. The effect of adrenin is evanescent; the effect of iodin is sustained; each in excessive doses causes acidosis: each in excessive doses causes histologic changes in the brain, the adrenals and the liver; and each causes many of the phenomena of emotion, exertion, injury, infection and Graves' disease.

Inhalation Anesthetics — Ether — Nitrous Oxid

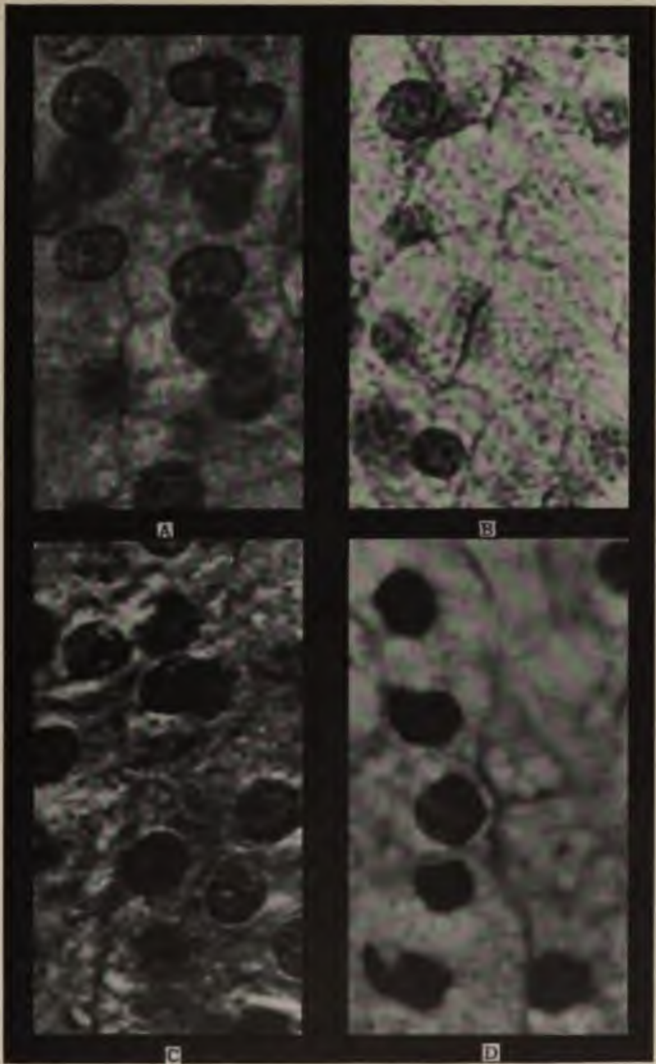
Although nitrous oxid and ether alike produce unconsciousness, the effects of their administration differ in certain respects. While we are not prepared to assign the cause of this difference, we can apply the test of histologic examination of the brain, the adrenals and the liver after the administration of each. Prolonged administration of ether produces histologic changes in these organs, corresponding in kind, if not in degree, to the histologic changes produced by strychnin, alcohol, acids, etc. After the prolonged administration of nitrous oxid, on the other hand, the cells of the brain, the adrenals and the liver are found to be hyperchromatic, as after the administration of morphia or sodium bicarbonate. Further evidence of the conservative power of nitrous oxid as compared with the de-



A. Section of normal cerebellum of a dog. B. Section of cerebellum of a dog after injection of diphtheria toxin. C. Section of cerebellum of a dog after injection of diphtheria toxin *plus* morphin. D. Section of cerebellum of a dog after injection of diphtheria toxin and the continuous administration of nitrous oxid for four hours.

FIG. 74.—PROTECTIVE EFFECT OF MORPHIN AND OF NITROUS OXID ON THE BRAIN-CELLS OF DOGS WHICH HAD RECEIVED INJECTION OF DIPHTHERIA TOXIN.

Compare the Purkinje cells in C and D with the disintegrated hypochromatic cells in B. (From photomicrographs, × 310.)



A. Section of normal adrenal of a dog. B. Section of adrenal of a dog after injection of diphtheria toxin. C. Section of adrenal of a dog after injection of diphtheria toxin *plus* morphin. D. Section of adrenal of a dog after injection of diphtheria toxin and the continuous administration of nitrous oxid for four hours.

FIG. 75. — PROTECTIVE EFFECT OF MORPHIN AND OF NITROUS OXID ON THE ADRENALS OF DOGS WHICH HAD RECEIVED INJECTION OF DIPHTHERIA TOXIN.

Note the general disappearance of cytoplasm and nuclei in B and compare with the normal appearance of C and the conserved nuclei in D. (From photomicrographs, × 1640.)

structive effect of ether was found in laboratory studies on the effect on animals of the simultaneous administration of an infection — diphtheria toxin — with ether or with nitrous oxid.

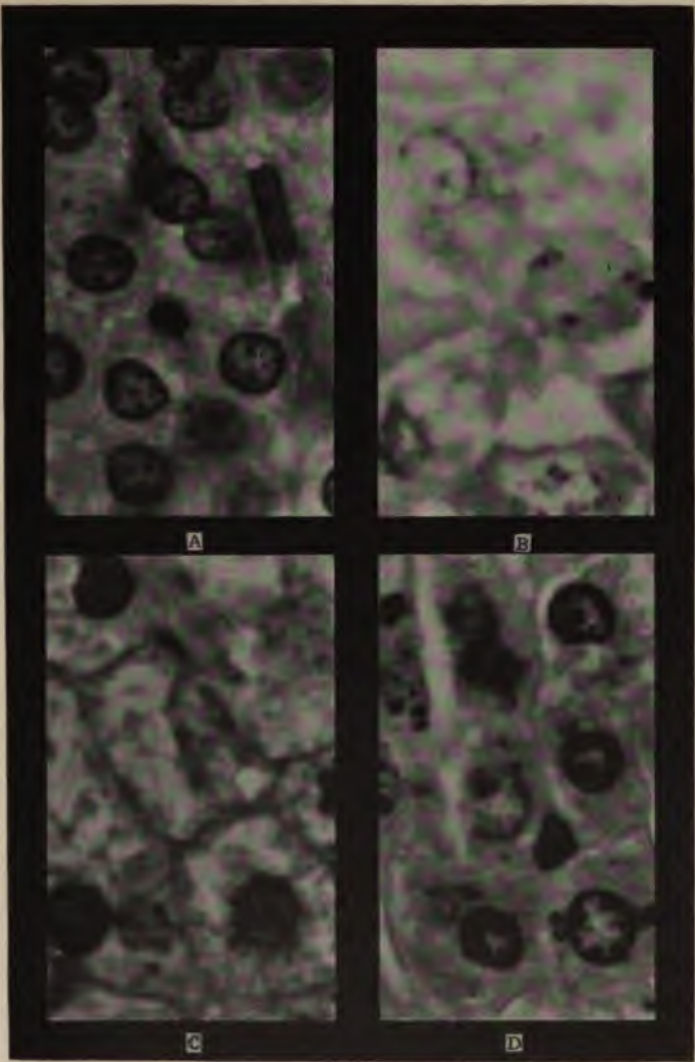
In animals which received a dose of diphtheria toxin and were kept under ether anesthesia for four hours, greater histologic changes were produced in the brain, adrenals and liver than were found in other animals given a like dose of diphtheria toxin but not anesthetized at all. On the other hand, in animals given diphtheria toxin and kept for four hours under continuous nitrous oxid anesthesia, the cells of the brain, adrenals and liver not only were unchanged, but in some instances were hyperchromatic, corresponding closely to the cells of these three organs in animals which had been subjected to diphtheria toxin and morphia, or to sodium acid phosphate and sodium bicarbonate. (Figs. 74, 75, 76.)

This evidence shows that by the simultaneous use of morphia and nitrous oxid, as in the operation under *anociation*, the greatest possible protection has been given to the kinetic system.

Summary

Thus, at will, by the administration of certain drugs, the kinetic organism of man and animals may be accelerated, retarded or its action suspended.

Thus, at will, by the use of drugs we may produce in the organism phenomena which resemble those produced by fever, infection, emotion, etc., and in like manner the phenomena of sleep or death may be produced.



A. Section of normal liver of a dog. B. Section of liver of a dog after injection of diphtheria toxin. C. Section of liver of a dog after injection of diphtheria toxin *plus* morphin. D. Section of liver of a dog after injection of diphtheria toxin and the continuous administration of nitrous oxid for four hours.

Fig. 76.—The Protective Effect of Morphin and of Nitrous Oxid on the Livers of Dogs which had received Injection of Diphtheria Toxin.

Note the vacuolation of B and compare with the conservation of nuclei and cytoplasm in C. (From photomicrographs, × 1640.)

CHAPTER XII

ACTION PATTERNS; CONSCIOUSNESS AND SLEEP

Action Patterns

WE know that the brain contains the mechanism that drives the body; we know that environment drives the brain and that environmental forces reach the brain through the mediation of the sense organs. But what is the mechanism within the brain by means of which a given stimulus causes different effects in different brains? Why will one man run away and another attack on receipt of identical stimuli?

We postulate that the adaptive reactions of the organism are executed by mechanisms, each of which, like a wireless station, awaits the arrival of the specific impulse which is to awaken it to specific response. Between the ceptor organs of the eye, the ear, the nose, the sensory nerve endings in the skin and the nerves governing muscles and glands there intervenes an intricate network of action patterns. As over the same copper wire may be transmitted the voice, a telegraph message, a dynamic charge of electricity for firing a mine, lighting a concert hall or driving an engine, — so over the same nerve or group of nerves may be transmitted impulses destined for the production of terror, of sudden flight or of the reactions of eating or drinking. Thus during consciousness the

brain is the seat of a continual flow of opposing, assisting, crossing and interfering impulses, the amount of fatigue produced being proportional to the number and strength of stimuli that evoke responses, whether these responses be those of gross activity or of mere perception.

It is not as difficult as it seems at first to conceive how the most complex reactions have been built out

FIG. 77. — CROSS-SECTION OF LEAF AND HAIR OF VENUS' FLY-TRAP.

Drawing showing the cellular mechanism which corresponds to the nerve path in animals. The expansion or compression of these cells, resulting from the touch of an insect, causes the leaf to close upon the insect in a few seconds, like a trap.

of the less complex by the simple process of multiplying the number and sources of stimuli. In the motor response of Venus' fly-trap we have a simple action

pattern. In my laboratory, Miss Menten identified the conducting path over which the stimulus apparently travels to the effector mechanism of Venus' fly-trap. (Fig. 77.) Here a response takes place by means of one continuous path of conduction without any break in its entire length. Without a brain or a nervous system, but with the equivalent of nerve fiber in the form of a tissue which contains lecithin-like compounds and salts similar to those in nerve tissue, the plant organism makes a response to an adequate stimulus as specific as are any of the responses made by man. When a fly alights upon the skin of man, it causes a tickling sensation and is immediately brushed off; when it lights upon the hairlike appendages of Venus' fly-trap, it is caught by the motor mechanism of the plant, bathed with digestive fluid and consumed. By an analogous process the same stimulus has caused two similar reactions in vastly dissimilar beings — one without a brain, the other with a brain. In one case the stimulus traveled to a central organ where energy was released which in turn activated a specific set of muscles to perform a specific act. In the second case the stimulus traveled directly to the effector mechanism, probably releasing energy along the way. In Venus' fly-trap but one receptor and one effector mechanism has been evolved for but one adaptive reaction. In man many receptor and effector mechanisms have been evolved for numerous reactions in response to numberless stimuli.

If it were necessary for Venus' fly-trap to catch its food by running instead of by passive attraction, the plant would doubtless have evolved a mecha-

nism coördinating the organism for running — in other words, a brain. The difference between Venus' fly-trap and man is the difference between the number of mechanisms possessed by each. A multiplication of the single action pattern of Venus' fly-trap equals the mechanism of man.

Pawlow has shown, in a recent work, that new reflexes may be created in an animal by superimposing new stimuli upon older ones, simultaneously with the occurrence of old reflexes. Thus, when a dog is being fed, if he be frequently subjected to a painful electrical stimulus applied to a given area of skin, a reflex to this electrical stimulus will soon develop which is precisely like that shown in response to the exhibition of food. This reflex, which corresponds to an action pattern, is termed a "conditioned" reflex, in contrast to the normal or "unconditioned" reflex.

As an explanation of the creation of the new reflex, Pawlow[1] states that the "nervous impulse resulting from the stimulus, which formerly went to a particular region of the nervous system, is now directed to a different one." He says: "In this way we have been able to direct the impulse from one path to another, according to the conditions; and we cannot avoid the conclusion that this represents one of the most important functions of the highest parts of the central nervous system."

In some such manner, doubtless by a slow and continuous process, the changing conditions of environment have superimposed new stimuli upon the old until by the infinitely varying stimuli which simul-

[1] Pawlow: The Investigation of the Higher Nervous Function.

taneously compete for entrance, the brain patterns of man have been modified and the complex reactions of social adaptations have succeeded the simple processes of food-getting and injury-avoidance which were sufficient for the primitive organism.

Theoretical Structure of Action Patterns — Effector Ceptors

The manner in which this vast multiplicity of adaptive responses is achieved and their specificity established may be inferred from the facts that the nerve paths over which impulses pass from the periphery to the brain are insulated; that the nerve paths over which pass the motor impulses from the brain to the periphery are insulated; and that the innumerable conducting paths in the brain are not insulated. From this arrangement we infer that it is necessary that impulses from the sense organs to the brain, and impulses from the brain to the muscles, be carried intact and undisturbed; whereas within the brain it is necessary — or immaterial — that impulses be disseminated freely.

Reflection upon these two opposite types of structure within the brain and without the brain suggests the following hypothesis regarding the manner in which action patterns are constructed.

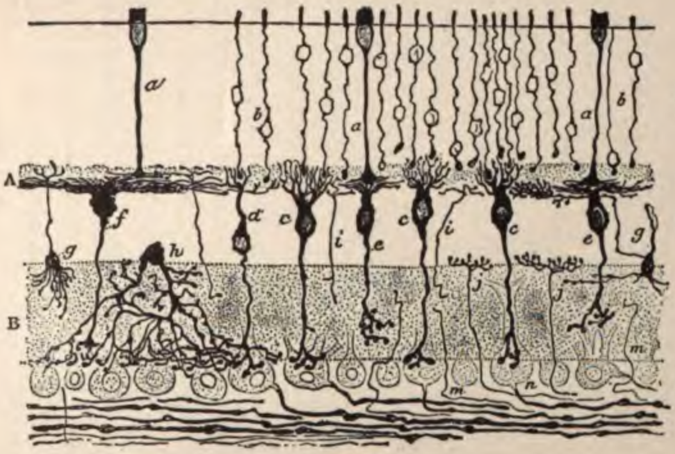
Let us suppose that the brain is composed of mechanisms of three general types, one for supplying motor power — the brain-cells; another for conducting this motor power as action currents; and the third, specific receptor mechanisms within the brain

whose function is that of receiving specific action currents — *effector ceptors*.

Furthermore, we may assume that these receptor mechanisms are endowed with the quality of being permanently modified by each impulse that passes over them, as a result of which the subsequent passage of an identical impulse is facilitated.

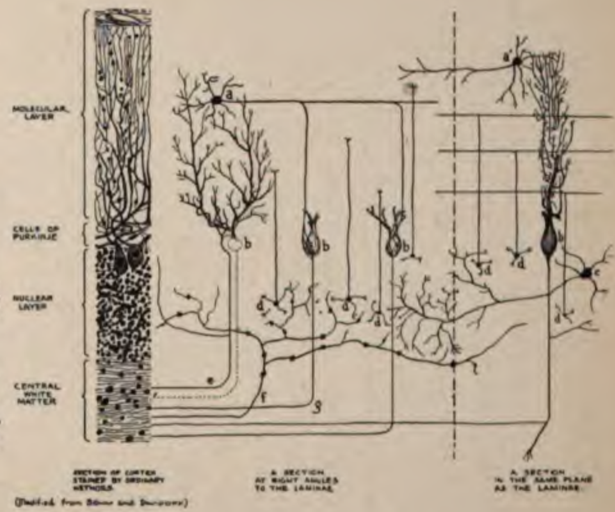
Our assumption is that the number and architecture of action patterns have been determined by natural selection; that no pattern exists but has selection value; and that all these patterns freely communicate with each other, and thus, indirectly, with all the cells of the brain. We suppose that in the brain there are millions of naked microscopic "wires," communicating with millions of microscopic "batteries" — the brain-cells. Thus among the brain-cells there is the freest possible intercommunication, and thus they communicate on the one hand with the sense organs through the peripheral nerve paths, and on the other hand through the specific receptors — *effector ceptors* — with the muscles of the body.

At first sight this hypothesis would seem to indicate chaos within the brain and confusion without. But how such an apparently chaotic arrangement could fabricate with precision the functions of the brain becomes evident when we recall that one of the first suggestions in our hypothesis was that all the multitude of action patterns were not fabricated at once, but that first one and then another action pattern was developed to meet the needs of the evolving organism, each new adaptation establishing its own path of least resistance so that now, although each



A.

(From Ramon y Cajal, 1894, Taf. V., Fig. 2.)



B.

(From Starling's "Principles of Human Physiology.")

Fig. 78. — Resemblance between the microscopic structure of the mechanisms in the eye *known* to be adapted for the reception of the specific energy of light (A) and mechanisms in the brain *postulated* to be adapted for the reception of specific action currents — *effector ceptors* (B). The free ends in each are not insulated; each communicates with nerve cells; each has obvious paths of communication with the remainder of the brain mechanism.

nerve impulse on reaching the brain *may* have access to any one of the innumerable patterns, entrance is secured to only that pattern by which the least resistance is offered. That is to say, whether an impulse shall pass over this or that or any action pattern depends upon the degree of resistance which has been established by the past experience of the organism; while the degree of vigor of the response depends upon the physical state of the brain-cells.

The assumption that by the lack of insulation each pattern is connected with every part of the brain — with all the brain-cells — suggests an explanation of the fact that all the energy of the brain may be drawn upon by any one or by a group of action patterns; thus, for example, the vigorous continuous use of the muscles of a hand or a foot may ultimately exhaust the entire brain.

The postulation of receptor mechanisms — *effector ceptors* — within the brain receives some support from the following arguments: (*a*) In some fish receptor mechanisms are known to exist in the brain; (*b*) the eye and other sense organs may be considered as receptor mechanisms projected outside of the brain; (*c*) the known receptor mechanism of the eye bears a resemblance to certain structures within the brain whose function may equally well be receptive (Fig. 78); (*d*) if the nerve receptor mechanisms of the eye, the ear and other sense organs are adapted to specific energies, why may not similar nerve structures within the brain likewise act as specific energy receptors? (*e*) if the sense receptor organs mediate between the external environment and the brain, why is it not

logical to assume the existence of receptor organs within the brain mediating between the inflowing impulses and the outgoing action currents?

The innumerable receptor mechanisms — *effector ceptors* — in the brain may be likened to hundreds of thousands of wireless receiving stations each of which registers only those messages received from the specific transmitter to which it is adjusted; or they may be compared to a vast number of tone receptors in a great chamber, each of which will deliver its specific note only in response to sound waves of a specific length and velocity.

In such manner one may suppose that each of the innumerable stimuli that reaches the brain activates only the action pattern which by that master-artificer — Environment — has been attuned to that stimulus.

Application of Theory of Action Patterns

If the predication of such a method of evolving character and individuality seems strange, it may be well to contemplate the steps by which man from the moment of his birth acquires the "experience" by means of which he is able to cope with environment.

There are first the simple reactions of sucking, crying, winking, sneezing. Gradually, more contacts, some beneficial, some harmful, are made. Objects and persons stand out from the chaos of surroundings, judged and catalogued by the one standard of *their effect on him* — the infant. We may suppose that each new contact writes a new record on the delicate matrix — a record of the sev-

eral stimuli which participate in the activation — especially the coincident stimuli of the distance and of the contact ceptors. Thus the sight of the mother and the sound of her voice are coincident stimuli with those of the acquisition of food — and, as in Pawlow's dog, the action pattern of acquiring food is in physical connection with the sight stimuli and voice stimuli of the mother. *Thus is associative memory developed.* Each new adequate stimulus writes a new record — begins a new action pattern — and when two or more stimuli act simultaneously the resultant pattern will ever after be activated in like manner by each stimulus. Thus in time, as one after another the contact stimuli of environment become associated with simultaneous distance ceptor stimuli, the action patterns are more and more activated by the associated distance ceptor stimuli alone. Thus step by step, action patterns made by the simultaneous stimulation of contact and distance ceptors become connected until in time activation is effected *almost completely through distance ceptor stimuli alone.*

After a contact with a given object has once been associated with a sight, a sound or a smell, the taste, smell or sight of that object will excite activity toward contact or away from contact according as the object is beneficial or harmful. For example, the contact ceptor stimulus of fire would be simultaneous with the distance ceptor stimulus of light and the action pattern of withdrawal would be stimulated. Subsequent to this association, the accompanying sight stimulus alone activates the moving-away action pattern — and the child therefore never again makes

contact with fire. The distance ceptor stimuli of light and heat take the place of contact ceptor stimuli.

On the other hand, let the infant be given a bottle of milk; it feels the bottle (contact stimulus); it sees the bottle, smells the milk (distance stimulus); the nipple is placed between its lips and the action pattern of sucking is excited. Thus the child obtains its first experience with a nursing bottle. The simultaneous repetition of the same contact and distance ceptor stimuli repeats the excitation of the same action patterns until in time the sight of the bottle alone stimulates the food-getting action pattern.

Thus from contact with each new factor in the environment, distance ceptor stimuli come to be interpreted in terms of contact ceptor stimuli. In like manner sign language, spoken language and written language at first were parts of action patterns which first were stimulated by contact ceptors. The beginning of mathematics is the action pattern of laying one block upon another. So the natural sciences have been evolved from the simple action patterns created by such stimuli as heat, cold, movement, weight, sound and light, by an ever increasing addition of associated action patterns. Thus too has been evolved the language of emotions. Education and training are probably the sum total of secondary action patterns introduced into the brain, and engrafted upon the original contact ceptor action patterns. Thus the action of the individual becomes inevitable; and by this conception we may interpret the life phenomena and actions of man and animals.

The action patterns of the child, which are wrought

upon its brain by contact with its immediate family environment, are permanent. Thus language, custom, religion, conduct and the conventions of races and peoples are transmitted through the generations. On the other hand, if a newborn Puritan babe, whose plastic brain has received no action patterns, were to be placed in the arms of a Patagonian Indian, its brain would receive and record the Patagonian language, customs and religion — and no other; and if that transplanted child remained until middle life exclusively in the new environment, no influence could take from that brain all the action patterns derived from that environment, though other action patterns might be superimposed.

The Hindoo, Chinaman, Brahmin, Teuton, Briton, Bushman, Christian or Pagan has acquired brain patterns which are ready-made by the environment into which he has been born and in the midst of which he has been reared; and not until the stronger stimulus of the necessity of race preservation intervenes will the old conventions, customs and languages give way to the new.

The plasticity of the brain may be observed on a large scale in the results obtained in the schools of a cosmopolitan city like New York, where the children of immigrants, drawn from all quarters of the globe from Iceland to Australia, are subjected to similar educational influences. The mass in the "melting pot," as it has aptly been termed, rapidly approaches a semblance of homogeneity, not alone in mental and moral characteristics but even in facial characteristics, as has been shown by students of physiognomy.

Polish, Russian, Jewish, Irish, English, German, Scandinavian, African, Spanish and Hindoo children rapidly lose their definite lines of demarcation under the steady drill of new teachings and new surroundings. When intermarriage shall have added its influence to that of education, the structural lineaments of race, as well as the customs and manners of these descendants of the first products of the melting pot, will in many essentials be indistinguishable from those of the descendants of the Mayflower pilgrims.

The greatest single influence in bringing about this leavening of the mass and the production of a common type of humanity is the spread of commercial interests and scientific knowledge. The new ideas, new customs, new languages, new religions and new inventions of invading strangers are accepted or rejected in the proportion in which they are indispensable to life. In proportion as the Mexican, the Hindoo, the Chinaman and the African need recreation, food, clothing and improved dwellings do they accept the American missionary or German hardware. One may interpret the habits, thoughts, customs and reactions of individuals, classes and races by the conception that they are produced by an activating environment playing on a plastic nerve mechanism, and producing action patterns whose responses to recurring stimuli are inevitable. As with Pawlow's dog, any set of action patterns may be modified by superadded associations.

Consciousness and Sleep

On the basis that the reactions of man and animals may be interpreted in terms of action patterns we may interpret the phenomena of consciousness and lack of consciousness or sleep.

With the first cry of the newborn babe in response to the adequate stimulation of its contact ceptors, begins the development of consciousness. Bright lights, certain sounds, the primary colors, the sun, the green fields, sky and water, animals, people; the experience of sitting erect, of creeping, walking and talking, of playing games, of the kindergarten; junior-grade sports; senior-grade duties; graduation; human relations; marriage, — all the experiences of life from moment to moment, from day to day, from year to year, add new action patterns. Thus as the human organism progresses from infancy to manhood new action patterns are constantly added to environmental contacts. The activation of these patterns constitutes man's conscious life. By this conception *consciousness is the response to environmental stimuli: sleep is the absence of response to environmental stimuli.*

For at least two months before birth, the fetus is ready to be conscious, but lacks the adequate environmental stimuli which cause the reactions of consciousness. The only difference between the unconscious fetus and the awake newborn babe is found in the few simple responses made by the latter to the stimuli of light, sound and physical contact.

As consciousness increases, motor reactions increase likewise, and the time consumed in sleep lessens.

In certain species of animals, the maximum of consciousness and minimum of sleep is established promptly at birth, owing to the requirements for nutrition and the necessity for an immediate motor adaptation against constantly menacing enemies. Only in those species in which the parents are able to defend their young against enemies and to supply them with food is there a period of prolonged unconsciousness after birth. Birds which nest in the branches of trees and are hidden from their enemies sleep much of the time during the first days after they are hatched; but birds which nest on the ground, and depend for safety upon their ability to run and hide from prowling enemies, are conscious and able to run almost as soon as they are hatched. For example, young quail are sometimes seen running about with pieces of shell still on their backs. Aquatic birds are awake and active as soon as they are hatched. The eaglet, on the contrary, which spends its early days on the inaccessible peaks of rocky promontories, develops slowly. The offspring of the herbivora are wide awake and able to walk, even to run, on the first day after birth. The herbivora are dependent upon flight for their safety; while the young of the carnivora, which are able to defend their offspring, sleep for days after their birth.

This, and the quality of food, may explain why the hunted herbivora eat more, and oftener, and sleep less than do the pursuing carnivora. The herbivora, needing to be constantly on guard, use more fuel and hence need to replenish their resources more constantly and abundantly; while the carnivora, secure from attack, divide their time between hunting and sleep-

ing, thus requiring a minimum of food — an advantage to the herbivora as well. Of all animals, the bird, perhaps, is the most intensely conscious: it transforms relatively the most energy and eats proportionally most of all.

In certain physiological states in which consciousness is at a low ebb because of age or disease, there may be noted a similar coincidence between diminished consciousness and diminished motor adaptation. In the senile, in the anemic and in patients with cerebral softening, or in whom the brain is compressed as the result of a hemorrhage or a tumor, there exists a state of diminished consciousness and a correspondingly limited capacity for muscular action which is analogous to these conditions in the newborn babe. It is of further interest to note, in this connection, that in these states of reduced consciousness, it requires but a small amount of an anesthetic or narcotic to produce unconsciousness or even death. In the aged, the anemic or the newborn, a small dose of morphia may be fatal. Conversely, the more intense the consciousness, whether from emotion or injury, the greater the amount of ether, nitrous oxid or morphia required to produce unconsciousness.

It would appear from these facts, that the mechanism which is specifically influenced by anesthetics and narcotics is the mechanism by means of which, in a manner as yet unknown, normal sleep is produced. It is obvious that consciousness is depressed in sleep; and that the phenomena of sleep — muscular relaxation, incoördination, diminished consumption of oxygen, diminished output of carbon dioxid, lowered

metabolism, diminished rate of pulse and respiration and lowered temperature and blood-pressure — are all phenomena of diminished consciousness. (Fig. 79.) That sleep only partially suspends the brain function is indicated by the fact that during sleep there may be a partial response to stimuli, such as is indicated by the shifting of posture and by moving in response to a call. It is particularly the function of the special senses which is suspended; and it is in response to stimulation of the special senses, as we have shown, that most of the energy of the body is expended. Nevertheless, even while the function of the special senses is suspended, there may continue in the brain a symbolic train of action in the form of word pictures or dreams which, if sleep be light, are recorded on the feeble consciousness of the sleeper and may be recalled on awakening. The subconscious memory of some dominating experience of the day may break through light sleep and cause a muscular response.

That the maintenance of consciousness requires a transformation of energy by the kinetic system is evidenced by the histologic changes produced by prolonged continuous loss of sleep in the organs of the kinetic system of rabbits, and in the fact that these lesions can be restored only during sleep; during unconsciousness produced by nitrous oxid anesthesia; or to some extent, when consciousness is depressed by morphia. Our experiments indicate that the lesions of the kinetic system produced by emotion, by exertion, by infection, like the lesions due to prolonged consciousness, are repaired only during sleep. During sleep, activating stimuli are apparently grounded.

Photo by Wm. J. Brownlow.

FIG. 79. — SLEEPING CHILD.

The energy expended in waking activities is being restored in sleep. Compare the relaxed position of the whole body as shown here with the muscular action in Fig. 82.

As daylight and darkness blend into one another by infinitesimal intervals, so that none may say where daylight ends and darkness begins, so consciousness and sleep blend into one another. The brain is the arena in which countless stimuli pass and repass, cross, combine, oppose and interfere, wax and wane in intensity, appear and disappear; now one gains the final common path, now another, thus creating an infinity of kaleidoscopic patterns, in which hopes and fears, desires, sentiments, actions, go to make up the manifold life — the consciousness of the individual. Life and adaptation to environment begin and end in unconsciousness. Unconsciousness is the basic state; consciousness is the evoked state. The sum total of consciousness is the sum total of the adaptive responses made by the kinetic system throughout the span of life.

And as these adaptive reactions vary widely from species to species, and from individual to individual, so consciousness varies. The newborn individual, like the individual weakened by some hereditary defect or disease, — the cretin, the victim of hypothyroidism or hypopituitarism, — cannot reach a useful height of consciousness, cannot attain a large sum total of consciousness. Likewise, the individual whose thresholds are low to only a limited number of stimuli reaches but a limited degree of consciousness within the limited environment which is open to him. The man whose mind is closed to the beauties of nature, music and art has a consciousness limited to an environment devoid of a number of activating stimuli. The musician, or any specialized worker who responds intensely, and for the most part only, to the stimuli

which are connected with his work attains to but a limited degree of consciousness, and is, so to speak, unconscious to most of his environment. That individual has lived most, has experienced the highest degree and the largest sum total of consciousness, who has responded most to the widest variety of stimuli; who has acquired and made use of the greatest number of action patterns.

CHAPTER XIII

PAIN, LAUGHTER AND WEEPING

Pain

THE specific response of *pain* to stimulation of the contact ceptors has been discussed in Chapter III. There we considered the distribution of pain areas; the types of contact ceptor stimuli that elicit pain; the specificity of the pain response to the exciting stimulus; and the fact that pain is always associated with a protective muscular action. It remains to consider the biologic utility and the mechanism of the pain which is elicited by pathologic conditions.

Here too the law of phylogenetic association is easily applied, for as response to contact ceptor stimulation is most intense in the parts most commonly subjected to attack and to physical injury, such as the tips of the fingers, the palms of the hands, the soles of the feet, the chest and the abdomen, while the deeply protected portions of the body, such as the liver, spleen, kidneys, brain and lungs are pain-negative, so a type of infection which is associated with pain when it involves one portion of the body may be painless when it involves another portion. Tuberculosis of the lungs, for example, is painless, while intense pain is associated with tuberculosis of the hip.

I believe it will be found, on careful analysis, that the infections which are associated with pain are those

in which there is *danger that the disease may be extended by muscular action, or in which fixation of the parts by continued muscular rigidity is of distinct advantage in overcoming the disease.*

In such diseases as scarlet fever, typhoid fever, measles, malaria, whooping cough, typhus, syphilis in the early stages, and in fact in most of the exanthemata in which the organism as a whole is quickly involved by the dissemination of infection, and in which muscular action can render no assistance, there is, as a rule, no pain. On the contrary, the infections generally associated with pain are the pyogenic infections, of which local inflammation, boils, carbuncles, felons and abscesses are common instances — infections the main characteristic of which is a local point of involvement or focus.

A fundamental and striking difference between the painless exanthemata and the painful pyogenic infections is found in the fact that, in the case of the former, the protective response of the body is wholly chemical — the formation in the blood of anti-bodies which usually produce a permanent immunity, while in the latter the defense is largely phagocytic. In the pyogenic infections, in order to protect the remainder of the body, which enjoys no immunity, every possible barrier against the spread of the infection is thrown about the local point of infection. Lymph is poured out and the part is fixed by the continuous contraction of the neighboring muscles and by the inhibition of those muscles which by the ordinary exercise of their functions would spread the disease. As would be expected, this continuous contraction is associated with pain.

Wherever a continued inhibition of muscular action in the vicinity of a local infection would be of no assistance in localizing the disease, or in those parts of the body in which muscular activity is a fundamental requirement of life — as, for instance, in the lungs — there pyogenic infection is unattended by pain. Thus, no muscular rigidity and consequently no pain is associated with pyogenic infections in the substance of the liver, in the substance of the kidney, within the brain, in the retroperitoneal space, in the lobes of the lungs, in the chambers of the heart or in the blood vessels of the chest or the abdomen.

Another type of pain, headache, more indirectly but none the less positively, modifies muscular action in the body. Headache is one of the most common initiatory symptoms of various infections, especially of those which are accompanied by *no local pain and no local muscular action.* On the other hand, headache is rarely associated with peritonitis, cholecystitis, pleurisy, arthritis, appendicitis, salpingitis, childbirth, obstructions of the intestinal and the genito-urinary tract — with any condition, in short, the local symptoms of which are overwhelming enough to govern the individual, *as a whole, to make him lie down and keep quiet, refuse food and possibly reject what is already in the stomach.* But in diseases in which the protecting local pain is absent, such as the exanthemata, typhoid fever, auto-intoxication, in which no dominating disturbance acts as a policeman to put the patient to bed and to force him to refuse food that he may be in a more favorable condition to combat the oncoming disease — in these conditions, headache serves a

beneficent and important purpose. The body, stricken by acute infection or poisoned by auto-intoxication, needs to rest and to fast; hence the entire muscular system obeys the command of this single pain, located in the controlling organ of the body, and muscular relaxation follows.

Strange and yet intelligible, in view of this conception, is the fact that, although a headache may be induced by even a slight auto-intoxication, an abscess may exist in the brain itself without causing pain. Inhibition of muscular action is a protection in one case; in the other it is useless. In like manner this principle may explain the acute pain that is present when an obliterative endarteritis is threatening a leg with anemic gangrene, or when one lies too long in the same position on a hard bed so that injury from local anemia threatens. But when the obliterative endarteritis threatens anemia of the brain, or when an embolism or thrombosis has produced anemia of the brain, there may be no pain, for muscular action, which in the former instance would be a protective response, in the latter would be of no use.

A most striking instance of the protective nature of pain is found in the phenomena of peritonitis. Through the law of natural selection, the peritoneum, in its relation to vast fields of possible infection, has become wonderfully endowed with mechanisms for resisting and overcoming infection. If the focus can be localized, almost any infection in the peritoneum can be overcome. This localization is accomplished by holding the muscular intestinal walls still and rigid against a large volume of gas, and by quickly throwing

out a fixative fluid or exudation. As a secondary adaptation, the stomach contents are ejected by vomiting, so that a protective anorexia against useless food also stands guard.

If our conclusions are correct, why are certain cases, familiar to every surgeon, of widespread general peritonitis, cholecystitis or of other abdominal lesions unaccompanied by pain, often without muscular rigidity or tenderness even, so that the surgeon may be misled in his diagnosis, and the result may be fatal? In seeking an explanation for these cases, which are almost invariably found either among the aged or the very young, we are led to formulate a postulate regarding the source or the site of pain.

The Site of Pain

If pain is a part of a muscular response and occurs only as a result of stimulation to muscular activity by physical injury, infection, anemia or obstruction, in what part of the nervous arc may the mechanism for the production of pain be found? Are the pain phenomena associated with the physical contact of the stimulus with the nerve ending; with the process by which the impulse is transmitted along the nerve trunk; or with the process by which the energy in the brain-cells is released and the impulse to the muscles is transmitted? It seems most probable that pain is associated with the discharge of energy by which the motor act is made possible.

If this be true, then, if every contact ceptor in the body were equally stimulated in such a manner that all stimuli reached the brain-cells simultaneously,

then the brain-cells would be in equilibrium and no muscular act — hence, no pain — would result. In the nearest approach to this hypothetical condition that we know — instances of sudden and widespread burning by fire — there is said to be no pain.

But if all the contact ceptors of the body but one were equally stimulated and this one stimulated more strongly than the rest, then the stimulus of the latter would gain possession of the final common path and would cause a given muscular contraction and a sensation of pain. It is well known that when a greater pain stimulus is thrown into competition with a lesser pain stimulus, the lesser is submerged. The schoolboy takes advantage of this fact when he initiates the novice into the mystery of the painless plucking of a hair. The simultaneous but severe application of the boot to the blindfolded victim solves the problem, and the hair is plucked painlessly through the triumph of the boot stimulus over the hair stimulus in the struggle for the possession of the final common path.

This hypothesis is supported also by the fact that strong contact ceptor stimuli are often dispossessed by distance ceptor stimuli in such a way that an injury which under ordinary conditions would cause great muscular contraction and consequent pain, is endured in apathy because of the victim's complete obsession by some emotional stimulus. Instances of this kind are seen in cases of self-inflicted torture among savage tribes; in fanatics while under the stimulus of religious zeal; in cases of physical injury received by persons obsessed by anger or fear; and, to a lesser degree, in sexual emotion. Soldiers in the

midst of a battle often experience no pain from a wound and may not know they are wounded until after the emotional excitation has worn off, when the sensation of warm blood on the skin may be their first warning of injury.

Dr. Livingstone, the African explorer, has testified to his complete unconsciousness to pain during his struggle with a lion. Although he was torn by teeth and claws his fear overcame all other impressions. Possibly the phenomena of hysteria may also be explained on this basis, as may the unconsciousness of passing events in a person in the midst of great and overwhelming grief. By constant practice the student may secure the final common path for such impressions as are derived from the stimuli offered by the subject of his study, and so be oblivious to his surroundings. Concentration is but another name for the exclusion of irrelevant stimuli from the final common path.

Since both psychic and mechanical stimuli cause motor phenomena by the excitation of precisely the same mechanism in the brain, and since the more rapid transformation of energy by psychic stimuli in these cases submerges the transformation of energy by physical stimuli and prevents pain, it would seem as if the phenomenon of pain must be associated with the process of releasing energy in the brain-cells and with the passage of energy to the effector mechanism — the muscles. Were a physical injury inflicted in a quiescent state equal to that inflicted without pain during a highly emotional state, there would result great pain and intense muscular activity.

Another viewpoint which throws further light upon

this hypothesis is well illustrated by the following case histories:

Several years ago, a man, 78 years old, whose chief complaint was obstinate constipation was admitted to the medical ward. The abdomen was but slightly distended; there was no fever; *no pain;* no increased leucocytosis; *no muscular rigidity;* and *but slight general tenderness.* The patient said he had lost in weight and in strength during several previous months. A tentative diagnosis of malignant tumor of the large intestine was made, but free movements were secured rather easily and we abandoned the idea of an exploratory operation. The patient gradually failed and died without a definite diagnosis having been made by either the medical or the surgical service. *At autopsy, there was found a widespread peritonitis arising from a perforated appendix.*

An infant was taken ill with some indefinite disease. Several of the ablest medical and surgical consultants of a leading medical center thoroughly investigated the case. Although they could make no definite diagnosis, they all agreed that surely it could not be appendicitis, because there was *no muscular rigidity* and *no tenderness. The autopsy showed a gangrenous appendix and general peritonitis.*

These two cases are illustrations of the principle that underlies the freedom from pain which results from the use of narcotics and anesthetics. It is the same principle that explains the fact that cholecystitis may occur in the aged without other symptoms than the presence of a mass and, perhaps, very slight tenderness. It accounts, in general, for the lack of

well-expressed disease phenomena in the senile and in infancy. The aged, the infant and the victim of general paresis show but few symptoms of disease because of the fact that in senility the brain is so deteriorated, and in infancy so undeveloped, that the cerebral mechanism of associative memory is inactive, hence pain and tenderness, which are among the oldest associations, are lacking. Senility and infancy are by nature normally narcotized. The senile is passing through the twilight into the night, while the infant is emerging from the shadows of dawn into the day. Hence it is, that in the extremes of life the diagnosis of injury and disease is subject to special difficulties. At such times, as regards symptoms, the entire body is as silent as the brain, the pericardium, the mediastinum and other normally symptomless areas. For the same reason, when a patient, seriously ill with a painful disease, turns upon the physician a glowing eye and an eager face, and remarks how comfortable he feels, then the end is near. The mechanism by which the transformation of energy is accomplished has run down. Energy is no longer available to register the results of stimulation in pain any more than in motion.

The most convincing evidence of this hypothesis, however, is found in the prevention of postoperative pain by the use of anociation. According to our hypothesis (explained at length in Chapter IX), postoperative pain is due to the state of low threshold established in the brain as a result of intense or repeated injurious impulses. The site of postoperative pain is not in the traumatized field, but in the brain. If the traumatic impulses are prevented from reaching

the brain by blocking the field of operation with local anesthesia, the brain threshold is not lowered, and there is consequently little or no postoperative pain.

There is a close resemblance between the phenomena of pain habit, of education, of physical training and of love and hate. In education, in pain habit, in all emotional relations, a low brain threshold is established which facilitates the reception of specific stimuli. All these processes are motor acts or are symbolic of motor acts. We may be trained to perceive misfortune and pain as readily as we are trained to perceive mathematical formulæ and moral precepts.

Laughter and Weeping

Much of the real nature of laughter and weeping, as of pain, is revealed by an examination of their distribution; that is, of the character of individuals among whom they are common, and of the situations to which they are incident. Laughter is an involuntary rhythmic contraction of certain respiratory muscles, accompanied usually by certain sounds. The motor act involves the respiratory apparatus primarily, but if the act is intense, it may involve not only the muscles of respiration, but also most of the other muscles of the body. There are many degrees of laughter, varying from a mere brightening of the eyes and a fleeting smile to intense hysterical and convulsive outbursts. From intense or prolonged laughter, even exhaustion may result.

Laughter is sometimes accompanied by the formation of tears and in many instances, in children especially, laughing and weeping are readily interchanged.

When strongly integrated to laughter, the nervous system can perform no other function.

According to Darwin, the only animals which laugh are men and monkeys. Other animals exhibit playful phenomena, and some exhibit certain types of facial expression which are associated with delight. But laughter, in the common sense of the word, is an attribute of the primates only; and even among men, proneness to laughter has a more or less limited distribution. It is more common, for instance, among healthy and happy, well-fed and comfortable individuals, than among the diseased, the oppressed and the poorly nourished. Laughter is more common among civilized than among savage races, and among highly intellectual individuals than among the stolid and crude inhabitants of the waste places of the earth. It is more frequent among individuals whose lives lie in the easy ways of luxury and leisure than among those whose waking moments are filled with an abundance of muscular activity. The Indian, the Eskimau, the Hottentot, laughs seldom, according to our standards. The Canadian woodsman, the mountain guide, the lonely cowboy, the range rider of the western plains, the heavy burden bearers of the Orient, the field workers among the poorer peasantry of the European countries, the women miners of Belgium, are all less prone to laughter — and also to weeping — than the excitable mental workers of American cities, or the lazy, well-fed and happy-go-lucky negro plantation 'hands.' The energy of the savage and of the "man with the hoe" like that of animals is preëmpted for a physical contest with nature. In the individual whose

life lies in softer places there is always an excess of energy above purely muscular needs.

Proneness to laughter and to weeping is modified by other conditions: by age, by sex, by training, by

Photo by Brown Brothers, N.Y.

FIG. 80. — LAUGHTER IN A HEALTHY CHILD.

An admirable illustration of the activation of facial muscles which is associated with hearty laughter.

mental states and, preëminently, by the state of health of the individual. Healthy, happy children are especially prone to laughter. (Fig. 80.) The aged

laugh less. Women laugh more than men. The healthy happy young woman on the verge of maturity laughs perhaps most of all, especially when slightly embarrassed.

What causes laughter? Good news, high spirits, tickling, hearing and seeing others laugh; droll stories; flashes of wit and passages of humor; averted injury; threatened breaches of the conventions; and numerous other causes. At first glance it would seem improbable that a single principle underlies all these diverse causes. Let us examine them, however, in the light of the fact that man is fundamentally a motor being, and that, in common with other responses to environmental stimulation, laughter is a muscular reaction.

We have postulated (Chapter III) that the laughter excited by adequate stimulation of ticklish areas of the body is a recapitulation of ancestral struggles against the physical attack of biting and clawing foes on these parts. In other words, the laughter excited by tickling is a substitute for the motor act of defense against injury, and is a reaction imposed by the need for giving vent to the energy mobilized in the kinetic organs at the command of the phylogenetic stimulus. The resultant action is purposeless, instead of purposeful; but the result in the expenditure of energy is the same. If the laughter excited be sufficiently intense or prolonged, the individual is as exhausted as if he had actually struggled with an enemy.

In like manner, the laughter excited by a psychic image is accompanied by a psychic conception, either clearly recognized or vaguely glimpsed, but none the

less an action pattern. We have shown (Chapter V) that emotions and psychic concepts, being responses to distance ceptor stimulation, are as truly representative of motor acts as are the responses to contact ceptor stimulation. Fear, anger and sexual love are representations of definite phylogenetic acts, which, if they do not follow directly upon the activating stimulus, leave the body in a physiological state of preparation for the act, which means that a certain amount of activating substances, which must be consumed or eliminated are thrown into the blood stream. If a motor act takes place in the midst of the emotion, the intensity of the emotion itself is lessened. A man in anger who fights, finds his anger dissipated as a result of his activity. A man in fear who flees, experiences less fear than he who waits motionless for the outcome of a situation.

The activating substances thrown into the blood by any emotion may be consumed as completely by any other muscular action, as by the particular muscular action for which these chemical substances were intended. On this principle, the purpose and cause of laughter and of weeping may be explained. If an individual be intensely provoked to anger, one of three things might happen: he might perform no physical act, but give expression to the emotion of anger; he might engage in a physical struggle and satisfy his anger; or he might immediately engage in violent gymnastic exercise which would consume the motor-producing elements mobilized in his body, and thus clarify the organism. Laughter and weeping are the gymnastic exercises which clarify the body under many

conditions of adequate stimulation to motor activity. Every one of the causes of laughter, when analyzed, resolves itself into a stimulation to motor activity of some kind.

Quite by accident this point was tested in our laboratory during the course of some experiments on fear. A keen, snappy fox terrier was completely muzzled by winding a strip of adhesive plaster around his jaws, so as to include all but the nostrils. He was then turned loose upon a rabbit. When the aggressive terrier and the rabbit found themselves in close quarters, the instinct of each animal asserted itself. The rabbit crouched in fear, while the terrier, with all the assurance of its kind when confronted by its natural prey, rushed upon the rabbit as if to seize it, his muzzle glancing off at each attempt and the attack ending in awkward failure. These actions were witnessed, at various times, by various scientific visitors, and in every instance the sight provoked laughter. This laughter was undoubtedly due to the fact that in the mind of each onlooker the spectacle of the savage terrier rushing upon the helpless rabbit as if to mangle it aroused a strong desire to exert a muscular act to prevent cruelty. This integration caused a conversion of potential into kinetic energy in the brain-cells, and a discharge of activating secretions into the blood stream, for the purpose of producing the muscular action. When the danger was unexpectedly averted, the preparation for muscular activity was appropriated by the neutral muscular reaction of laughter.

In children, almost any unexpected phenomenon,

such as a sudden "booing" from behind a door, will provoke laughter. In like manner, in an adult, a suddenly averted threat of danger, a breach of the conventions, sudden relief from acute nervous tension, a surprise, — indeed, any excitant, for which there is no predetermined method of physical response, — may give rise to laughter. In the same way the laughter evoked by jokes may be explained. An analysis of a joke shows it to be composed of two parts, — a first part, in which is presented a stimulus to action; and a second part, in which the story suddenly turns so that the stimulus to action is unexpectedly withdrawn; and so there are jokes of the classes — bankers' jokes, politicians' jokes, professional men's jokes, etc. The stimulus which excites one to action, by reason of his permanent brain patterns, fails to elicit response from another collection of brain patterns, as the foe of one animal fails to inspire fear or resentment in another whose path it seldom crosses.

It is interesting to note that the respiratory system, principally, is utilized for the muscular clarifying purpose of laughter. Why are not other muscular portions of the body utilized? Why do we not laugh with our feet and hands as well? As a matter of fact, the by-products of excitation are often consumed in other motor acts than those accompanying laughter, as is shown often in public gatherings by the stamping of feet and clapping of hands of an audience excited or amused by the impassioned or humorous words of a speaker; or by the activations of enthusiastic spectators at a championship ball game as pictured in Fig. 81. To be a truly adaptive phenomenon, however,

Photo from Brown Brothers.

FIG. 81. — BASEBALL FANS AT A CHAMPIONSHIP GAME.

An admirable illustration of the fact that the body-wide activation to motor activity, which accompanies laughter, often finds expression in motion of the hands and feet and of other portions of the body.

laughter must not seriously interfere with any other function. Were laughter expressed with the hands only, arboreal man might have fallen from the tree; and if expressed by the feet, our equilibrium might be lost. Laughter, therefore, is expressed by means of a group of powerful muscles which can be spared easily without seriously interfering with the maintenance of posture or any other function. In order that the products of excitation may be quickly and completely consumed, the powerful group of expiratory muscles must have some resistance against which they can exert themselves strongly and at the same time provide for adequate respiratory exchange. The intermittent closure of the epiglottis serves this purpose admirably, just as a horizontal bar affords the resistance against which the muscles of the athlete may be exercised.

Weeping, like laughter, is a part of the reaction to a stimulation to some form of motor activity, which may or may not be performed. (Fig. 82.) Take the case of a mother anxiously watching the course of a serious illness in her child. If, in caring for it, she is stimulated to the utmost to perform motor acts, she will continue in a state of motor tenseness until one of two events occurs — recovery or death. If relief be sudden, as in the crisis of pneumonia, and the mother is not exhausted, she will easily laugh. If tired, she may cry. If death occur, however, the stimulus to motor activity is suddenly withdrawn and she cries aloud and may perform many motor acts as a result of the stimulation to motor activity which is no longer needed for the physical care of her child.

A. B.

FIG. 82. — CRYING CHILD.

This baby's bottle was taken away from him and held, at first, just beyond his reach, when the desire to obtain it was expressed by a weak whimper and a placing of his hands in position to receive it back (A). Then, when the bottle was removed completely from sight, his activation increased and expressed itself in loud cries and rapid movements (B).

It is the common experience of every one to find that *during* a period of intense activity or intense integration to activity, as in a great catastrophe or misfortune, that the power to laugh or weep has disappeared. As soon as the issue that causes the integration is determined — the terror past or the doubt removed — the whole being seems to dissolve in one tremendous outburst of tears or laughter, with the result that the organism is in part immediately relieved.

With this key, we can understand why laughter and crying are so closely associated, and so frequently interchangeable under the same conditions; why either gives a sense of relief after stress; and why neither can come until the issue which has precipitated the activation has been settled. We can understand why an averted breach of the conventions, which would have caused embarrassment, may excite laughter; and why the recital of heroic deeds of a certain type causes tears.

Nowhere could this fact be more strikingly manifested than in the scenes of desolation and wretchedness described by eyewitnesses of the physical and psychic results wrought by the present War of Nations in Europe. The characteristic of the people that most impresses all chroniclers is the calm, the apathy of those who have undergone physical injury or psychic stress. In the midst of battle, no one weeps; no one laughs; every one is integrated for muscular action, for killing or escaping. The crushing of Belgium caused no weeping until the refugees had reached a safe haven. Then they wept abnormally. I saw striking instances of this.

These are illustrations of the principle which we have sought to make clear in the foregoing chapters — the fact that the nervous system acts *as a whole;* that it can respond to but one stimulus at a time; and that when the nervous system is preëmpted by one stimulus to the point of exhaustion, it can respond to no other until an approximately normal condition of the kinetic system has been regained through rest. The lack of the power to laugh or weep, and the absence of pain among the exhausted, the senile and those weakened by disease demonstrate the fact that the kinetic system is exhausted; that it has been integrated for response to a stimulus stronger than that to a motor activity for which laughter or weeping is a relieving substitute; and that consequently the energy required for laughter or weeping is no more forthcoming than it is forthcoming for any other form of motor activity under the same conditions.

A striking contrast to the absence of laughter or weeping when the brain thresholds have been raised by extreme exhaustion is found in the hypersusceptibility to both laughter and weeping, shown in cases of Graves' disease and in neurasthenia, both of which are inevitably marked by weak inhibition and a low threshold to all stimuli.

In Graves' disease the motor mechanism is in an exalted state of activity. These patients, therefore, as would be expected, exhibit an extreme susceptibility to laughter and weeping because of the fact that the motor mechanism is constantly integrated by the most trivial stimuli. In Graves' disease the flood gates of tears are open. The susceptibility to pain is also

intensified; and in these patients surgical shock is produced with abnormal facility. In the neurasthenic whose threshold also is low to stimuli, the discharge of energy in pain or laughter is equally facilitated.

Since pain, like laughter and weeping, is a motor phenomenon, it is not surprising that where pain does not give rise to muscular activity, it frequently leads to weeping.

CHAPTER XIV

TRANSFORMATION OF ENERGY AND ACIDOSIS

The blood of man, under normal conditions, is slightly alkaline with a hydrogen-ion concentration of about 7.56 in terms of Sörenson's logarithmic notation. But although in circulating blood the H-ion concentration upon which the amount of acidity depends is little more than that of distilled water, the blood is potentially much more alkaline than water, being able to neutralize a considerable amount of acid. At the time of death, from whatever cause, the concentration of H-ions in the blood is increased, the potential or actual alkalinity is decreased, and the blood becomes, in fact, neutral or acid. In order to discover what conditions tend to diminish the normal alkalinity of the blood, observations were made for me in my laboratory by Dr. M. L. Menten, Dr. W. J. Crozier, Dr. W. B. Rogers and Dr. B. I. Harrison, using electrical and chemical methods for determining the H-ion concentration of the blood under certain pathologic and physiologic conditions. As a result of these researches we are able to state that the H-ion concentration of the blood is increased by *excessive muscular activity;* by *excessive emotional activation;* by *surgical shock;* by *asphyxia;* in *strychnin convulsions;* by *inhalation anesthetics;* in the *late states of life after excision of the pancreas, of the liver* and

of the adrenals; and by *the continuous infusion of adrenin solution.*

On the other hand, the administration of morphia causes no change in the H-ion concentration of the blood nor does decapitation, provided artificial respiration is maintained.

Many observations were made on animals near death from various causes. In each instance the blood became increasingly acid as death approached. This fact suggests the following question: Is the termination of life in many diseases, such as infections, Graves' disease, shock, etc., due to the failure of the body to maintain its alkalinity? Certain facts seem to support an affirmative answer to this question, namely: (1) the intravenous injection of certain acids causes death quickly; and (2) the intravenous injection of acids causes extensive histologic changes in the brain, the adrenals and the liver, which resemble the changes invariably caused by excessive activation of the kinetic system.

Certainly it would seem as if anesthesia and many instances of unconsciousness are associated with increased H-ion concentration of the blood. As previously stated, we found that the H-ion concentration of the blood is increased by alcohol, by ether and by nitrous oxid. In addition, we found that the increase in H-ion concentration was more gradual under ether administration than under nitrous oxid, an observation which accords with the fact that nitrous oxid induces anesthesia more quickly than does ether.

Williams has found that in animals under ether anesthesia no nerve currents are detected by the

Einthoven string galvanometer. If we postulate that a nerve current can pass from the brain to the muscles and glands only if there be a certain difference in potential between these parts, the absence of a nerve current in anesthetized animals may be explained on the basis that any change in the normal alkalinity of the body would diminish the difference in potential; and hence the acidity produced by inhalation anesthetics would so far decrease the difference in potential as to inhibit the passage of the nerve impulse.

According to this hypothesis, as long as life exists, a string galvanometer of sufficient delicacy should detect a nerve current between the brain and the muscles and glands, that is, until the acidity is sufficiently increased to reduce the difference in potential to zero or the death point. During sleep one would expect a diminished flow of action currents. Blood taken from a sleeping man showed normal H-ion concentration. The histologic changes in the brain, the adrenals and the liver, produced by acid sodium phosphate apparently, are not repaired during rest without sleep, *but are repaired during sleep.*

Acidosis, therefore, may be caused by an intake of a smaller amount of alkalies and bases than are required to maintain an alkaline or neutral state; by an excessive rate of acid production; or by interference with one or more of the organs of acid elimination.

This conception of the relation of acidity to anesthesia and unconsciousness harmonizes many facts. It explains, for instance, how asphyxia, overwhelming emotion or excessive muscular activity, by causing acidity, may produce unconsciousness. It explains

the acidosis resulting from starvation, from uremia, from diabetes or from Bright's disease; and supplies a reason why the use of intravenous infusions of sodium bicarbonate sometimes overcomes the coma of diabetes and uremia. It may explain the quick death from chloroform, ether and nitrous oxid, and may, perhaps, suggest why unconsciousness is so commonly the immediate precursor of death.

One of the most noticeable immediate effects of the administration of an inhalation anesthetic is a marked increase in the rapidity and amplitude of the respiration. The respiratory center has evidently been evolved to act with increased vigor proportional — within certain limits — to the increase in the H-ion concentration, whereas the centers governing the voluntary muscles are depressed with the increase in H-ion concentration. In these antithetic reactions of the higher cortical centers and the lower centers in the medulla to acidity we find a remarkable instance of adaptation, by which the animal is prevented from killing itself through the further increase in acidity which would result from *continued excessive muscular activity.* In other words, *as the acidity produced by muscular activity increases and threatens life, the respiratory action, by which carbon dioxid is eliminated and oxygen supplied, thus diminishing the acidity, is increased, while the driving power of the brain, by which acidity is produced, is lessened or inhibited, producing unconsciousness.* Without this life-saving regulation, animals under stress would inevitably commit suicide. Direct chemical evidence supports the postulate that the cortical centers and the centers in the medulla

have been evolved to react to acidity in opposite ways; namely, the histologic changes in the several parts of the brain, produced by the intravenous injection of hydrochloric acid, acid sodium phosphate, etc., and by such acid-producing work as muscular exertion, emotion, physical injury, etc., are uniformly unequal. *These changes are striking in the cerebral cortex and slight in the medulla.*

It is probable that the remarkable phenomenon of anesthesia — the coëxistence of unconsciousness and life — is made possible by this antithetic relation between the cortex and the medulla. Within a few seconds after the beginning of nitrous oxid anesthesia the acidity of the blood is increased. This rapid acidulation is synchronous with almost instantaneous unconsciousness and increased respiration. If the amount of oxygen in the inhaled mixture be increased, a decrease in acidity occurs, together with lighter anesthesia and a decreased respiratory rate.

If our premises are sound, we are justified in concluding that the state of anesthesia is in part, at least, the result of an induced acidity of the blood. If the reduction of alkalinity be slight, then the anesthesia is light, and the force of the nerve impulses is lessened, but the patient is still conscious of them. As the alkalinity of the blood continues to decrease, associative memory is lost, and the patient is said to be unconscious; the centers governing the voluntary muscles are not wholly inhibited, however, since cutting the skin causes movements. If the alkalinity be further decreased, there is loss of muscular tone and even the strong contact ceptor stimuli of a surgical operation do

not cause any muscular response. And, finally, the acidity may be increased to the point at which the respiratory and circulatory centers can no longer respond, and anesthetic death — that is, *acid* (?) death — follows. It should be admitted, however, that increased acidity and its phenomena may be end-effects and not causes of anesthesia.

Opposed to this postulate is the fact that the injection of sodium bicarbonate does not overcome inhalation anesthesia. Possibly there may be intracellular acidosis which is not easily overcome by alkalies. How valuable this fact may be, I do not know. Certain clinical phenomena are clarified, however, by this postulate, and support it. For example, it is well known that inhalation anesthesia precipitates the impending acidosis which results from starvation, from extreme Graves' disease, from great exhaustion, from surgical shock and from hemorrhage, or when an animal is near death from any cause.

In striking contrast to the action of inhalation anesthetics, deep narcotization with morphin and scopolamin is induced slowly and the respiratory and pulse rates are progressively lessened. In addition, our experiments have shown that no increase in the H-ion concentration of the blood is produced by morphin or by scopolamin, no matter how deep the narcotization. In animals already narcotized by morphin, the production of acid by any of the acid-producing stimuli was delayed or prevented. On the other hand, in animals in which an acidity had already been produced by ether, shock, anger or fear, the *administration of morphin delayed or prevented entirely the neutralization of the acidity.* In

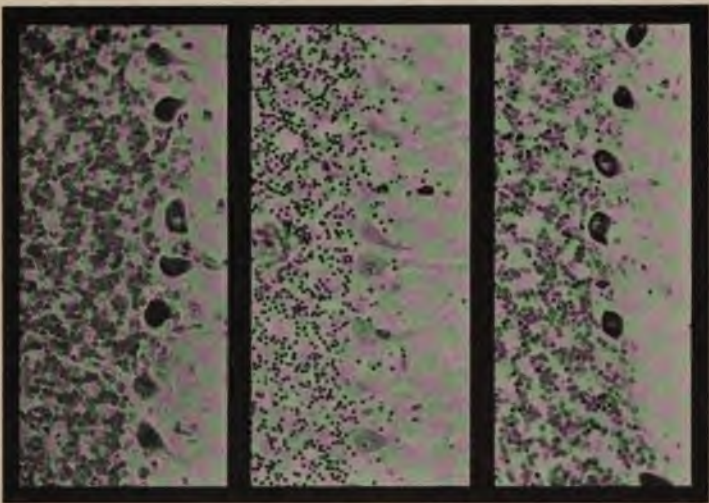
other words, morphin interferes with the normal mechanism by which acidity is neutralized, *possibly* because its depressing action on the respiratory center is sufficient to overcome the stimulating action of acidity on that center, for, as we have stated, the neutralization of acidity is in large measure accomplished by the increased respiration induced by the acidity itself; possibly also *because morphin prevents the output of adrenin*, and adrenin measurably governs the great acid-reducing organ — the liver.

Acidosis in Relation to Normal and Pathologic Phenomena

If, as is now believed by physiologists, the respiratory center is governed by the H-ion concentration of the blood, rather than by the want of oxygen merely, then the elimination of the by-products of metabolism is of paramount importance in the maintenance of the health of the organism; and its clinical significance, as pointed out by many observers, notably Fisher, Henderson and Michaelis, is obvious at once.

In my laboratory many observations have been made to determine the effect of the excision or functional depression of certain organs on the normal reaction of the blood and of the urine. When the liver is excised, the alkalinity of the blood is rapidly diminished and death follows. When the adrenals are excised, the blood maintains its normal reaction for a longer time — perhaps twice as long — but then its acidity increases rapidly and death follows. (Figs. 83, 84.) When connection between the brain and the remainder of the body is broken at the medulla, the blood remains normal

for as long as eight hours and shows no tendency to increased acidity. When the thyroid, spleen, testicles, kidneys, uterus, stomach or intestines, in short when any other organ than the adrenals, the liver or the



A. Section of normal cerebellum of a dog.

B. Section of cerebellum of a dog after double adrenalectomy.

C. Section of cerebellum of a dog after double adrenalectomy followed by injections of sodium bicarbonate.

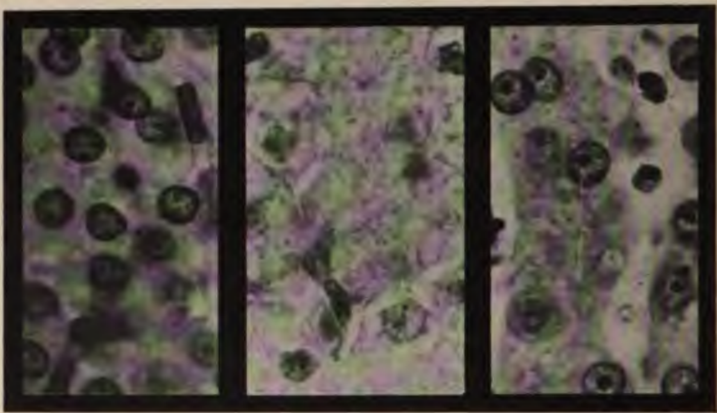
FIG. 83. — THE PROTECTIVE EFFECT ON THE BRAIN-CELLS OF A DOG OF INJECTIONS OF AN ALKALI AFTER DOUBLE ADRENALECTOMY.

Note the disintegration and disappearance of Purkinje cells in B and the normal intact condition of the Purkinje cells in C. This and the following figure demonstrate the neutralizing function of the adrenals.

(From photomicrographs, × 310.)

pancreas is removed, there is no tendency to immediate acidosis. Apparently, therefore, only the liver, the adrenals and the pancreas are principally engaged in the preservation of the normal alkaline reaction of the body fluids. The respiratory system eliminates the

gaseous by-products of energy transformation; the kidneys eliminate the acid salts in solution; the liver reduces the acid by-products to render them suitable for elimination by the kidneys; the adrenals measurably govern the liver and perhaps the *oxidation process required for the reduction of acid by-products.* Oxygen



A.	B.	C.
Section of normal liver of a dog.	Section of liver of a dog after double adrenalectomy.	Section of liver of a dog after double adrenalectomy followed by injections of sodium bicarbonate.

Fig. 84. — The Protective Effect on the Liver of a Dog of Injections of an Alkali after Double Adrenalectomy.

Note the disappearance of cytoplasm and of nuclei from B as compared with the normal and numerous nuclei and the conserved cytoplasm in C.

(From photomicrographs, × 1640.)

is apparently necessary in some way to acid elimination, just as oxygen is necessary to energy transformation. Adrenin also is necessary to both.

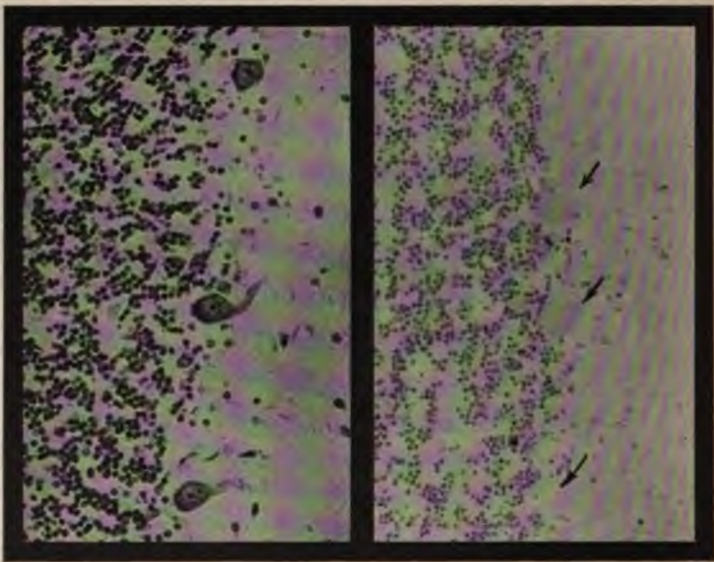
Let us examine some of the phenomena of normal and pathologic activation in the light of this hypothesis that acidity is the cause, rather than the result, of death;

that acidity blocks, as it were, the electrical discharge from the brain, which constitutes the principal attribute of life itself.

The respiratory rate is governed by the changes in the H-ion concentration of the blood, which result from energy transformation in the body; the pulse rate — provided local organs are normal — and also the temperature vary with the respiratory rate. We know that certain diseases are caused by failure of the organism to eliminate acid by-products. Bearing these facts in mind, let us examine the phenomena of several forms of activation. In great exertion the characteristic phenomena are rapid respiration, rapid pulse, sweating, redness of the skin, thirst and a progressive exhaustion. In the great emotions, emotions sufficiently intense to overwhelm the individual, the characteristic phenomena are the same — rapid pulse, sweating, flushing, thirst and exhaustion. These two normal states closely resemble each other. Do they in turn resemble the phenomena of certain pathological states?

Note the phenomena of fever. In the infections the leading symptoms are increased respiration, increased pulse rate, sweating, flushed face, thirst and exhaustion. In Graves' disease the leading symptoms are the same. Thus four comprehensive and typical conditions — exertion, emotion, infection and Graves' disease — have certain phenomena in common, a fact which strongly suggests *that these phenomena result in a large measure, at least, from the physical and chemical work involved in the elimination of acid by-products.* (Fig. 85.)

Granting this, we can understand clearly why acidosis is so frequently seen in severe cases of Graves' disease and why acidosis results from violent fever. We can understand the occurrence of albumin and casts in the



A. Section of normal human cerebellum. (After accidental death.)

B. Section of human cerebellum after death from acute acidosis.

FIG. 85. — EFFECT OF ACUTE ACIDOSIS ON THE BRAIN-CELLS OF A HUMAN BEING.

In B note the complete disintegration of the Purkinje cells of which but faintest traces remain. (See arrows.)

(From photomicrographs, × 310.)

urine as a result of exertion or emotion and in Graves' disease.

The H-ion Factor in Graves' Disease

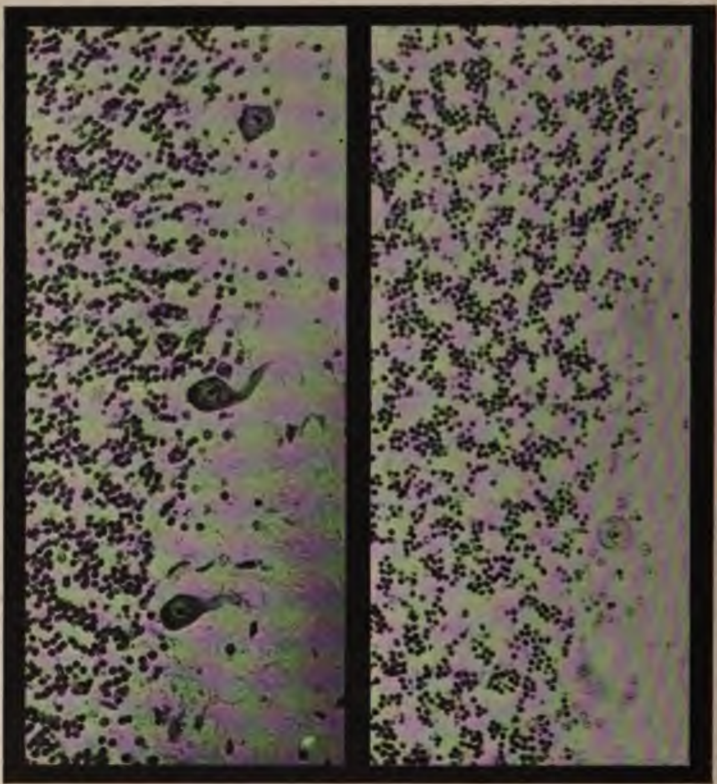
Having noted that the symptoms of Graves' disease resemble closely those of extreme exertion, of intense

emotion and of violent infection, we now offer the following interpretation of these phenomena.

Whenever there is an increased transformation of energy, the H-ion concentration of the blood is increased. As shown by Du Bois, in Graves' disease there is a continuous increased transformation of energy, hence an increased production of acid, and, consequently, an increased demand upon the acid neutralizing power of the body.

Let us now consider the symptoms in Graves' disease that may be due to acidosis in contradistinction to the symptoms that may be due to the activation of the kinetic system. As we have stated, H-ion concentration is controlled by three agencies: first, the elimination of carbon dioxid by means of the respiratory organs; second, the breaking down of the acid by-products of energy transformation by the liver; and third, the elimination of the acid by-products by means of the kidneys and skin. In Graves' disease the continuous excessive transformation of energy steadily reduces the neutralizing bases stored in the body until acidosis automatically results from the loss of neutralizing material. In addition, in Graves' disease the most important neutralizing organ — the liver — is greatly impaired — brown atrophy. The symptoms of so-called hyperthyroidism differ very little if at all from the symptoms of straight acidosis. This being so, does it not follow that postoperative hyperthyroidism is in fact an acidosis?

The symptoms of acidosis are increased respiration, increased sweating, loss of mental and muscular power, restlessness and, in extreme cases, delirium and uncon-



A.

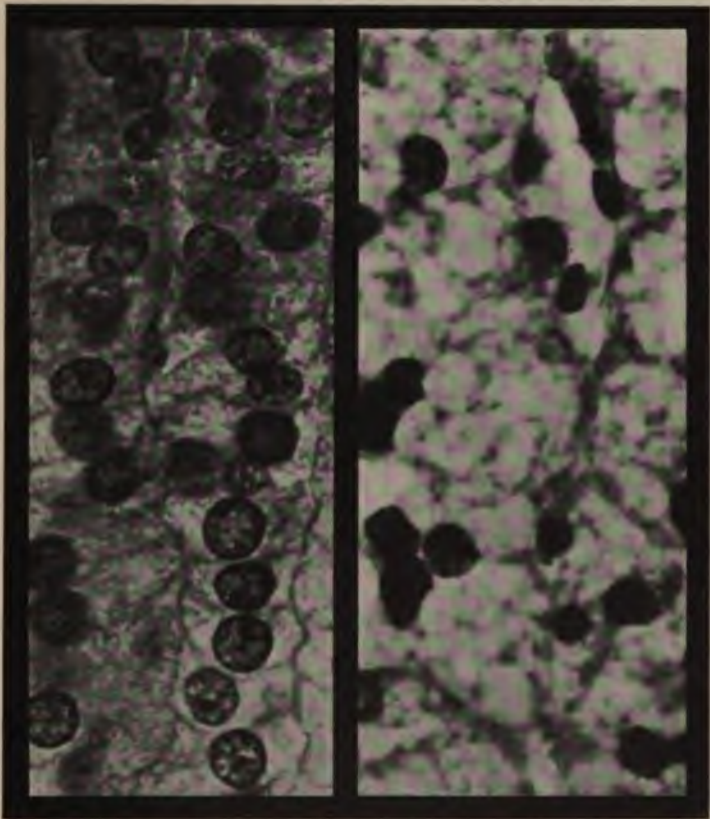
Section of normal human cerebellum.

B.

Section of cerebellum of a soldier who had suffered from hunger, thirst and loss of sleep; had made the extraordinary forced march of 180 miles from Mons to the Marne; in the midst of the greatest battle in history was wounded by the explosion of a shell; lay for hours waiting for help, and died from exhaustion soon after reaching the ambulance. Compare the faded-out exhausted Purkinje cells with the Purkinje cells in A.

FIG. 86. — EFFECTS OF EXTREME ACTIVATION ON THE BRAIN-CELLS OF A SOLDIER.

(From photomicrographs, × 310.)



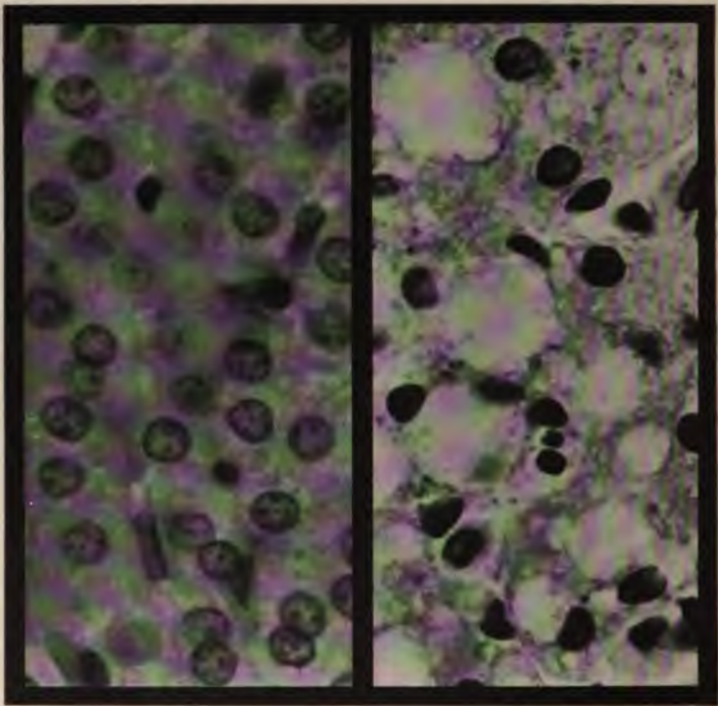
A. Section of normal adrenal.

B. Section of adrenal of soldier described in Fig. 86. The general disintegration of the cells, loss of cytoplasm, misshapen and eccentric nuclei illustrate the effect of emotion, exhaustion, lack of sleep, pain and trauma.

FIG. 87. — EFFECTS OF EXTREME ACTIVATION ON THE ADRENALS OF A SOLDIER.

(From photomicrographs, × 1640.)

sciousness. The increased temperature, increased pulse rate, flushed face and flushed extremities are identical with the symptoms of so-called hyperthyroidism.



A.
Section of normal liver.

B.
Section of liver of soldier described in Fig. 86. The general disintegration of the cells, the loss of cytoplasm, and the vacuolated spaces within the cells illustrate the effect of emotion, exhaustion, lack of sleep, pain and surgical trauma.

Fig. 88. — Effects of Extreme Activation on the Liver of a Soldier. (From photomicrographs, × 1640.)

Furthermore, as postoperative hyperthyroidism develops and continues, practically always a stage super-

venes in which there is acetone in the breath, and diacetic acid in the urine — a true acidosis.

The assumption that postoperative hyperthyroidism is a true acidosis explains also why it is that just before death in fatal cases of Graves' disease the temperature may rise as high as 107, 108 and even 109 degrees. It is because the long period of relative acidosis before the operation together with the increased acidity resulting from the operation, has taken away from the body the safe margin of neutralizing bases and alkalies and therefore the neutralizing bases in the living protein molecules are seized by the acids. This chemical process of breaking down the living protein molecules liberates heat. This heat is the chief cause of the rise in temperature before death. We know that when the temperature rapidly rises after a period of acidosis the living molecules are breaking down — and the end is near.

Summary

The establishment in the body of so powerful a group of organs and mechanisms for the elimination of the acid by-products of energy transformation shows how vitally necessary is the maintenance of the normal slightly alkaline reaction of the body. This indicates that acidosis is a factor in many diseases — acute and chronic — and that the centers in the medulla are stimulated by acidosis while the higher centers are depressed; it *suggests* an explanation of the phenomena of anesthesia, and that the ultimate cause of death is usually acidosis. (Figs. 86, 87, 88.)

CHAPTER XV

ELECTRO-CHEMICAL PHENOMENA

Physicists tell us that, in the last analysis, the primal stuff alike of matter and of energy is electricity. Whatever may be the superficial aspects of man's form and functions, ultimately they are phenomena of electricity. We may well ask, therefore: *Is the transformation of energy by which men and animals are enabled to adapt themselves to their environment effected through an electro-chemical mechanism?*

If this be true, there should be evidence to show: (1) that electricity is produced in the body; (2) that a current of nerve action, an electrical phenomenon, always accompanies the passage of the nerve impulse; (3) that in motor organs the electro-motive force of this current varies with the rate and extent of energy transformation; (4) that when there is no transformation of energy, there is no action current; (5) that electricity alone, either directly or indirectly, can excite various organs and tissues to perform their function; (6) that in the body are structures well suited to be parts of an electro-chemical mechanism which is capable of performing the work of the body; and finally (7) that no other form of mechanism is capable of performing this work.

One of the oldest established facts in the physiology of plants and animals is the fact that there is an electro-

negative variation during action. This was long ago studied in the sensitive plant. Bose has shown that electric currents are present in all plant activities. He has plotted curves of electric variation corresponding to periods of activity and of rest, and has shown that life and electric phenomena end simultaneously. Osterhaut has shown that the normal electric phenomena in kelp are changed by anesthetics, by iodin, by acidity and by varying the concentration of sodium, potassium and magnesium salts in the solution in which the kelp is immersed. He showed that the permeability of the plant cells varies with the activity of the plant, and that at death this electric phenomenon disappears. He also showed that the amount of energy in plants corresponds with the degree of permeability to electric currents at the surfaces of plant cells. R. S. Lillie established similar facts regarding the permeability of the larvæ of the marine worm, *Arenicola*. Lillie and Osterhaut believe that the electric phenomena of life in animals and plants are dependent upon changes in the permeability of the semi-permeable membranes which surround vegetable and animal cells.

Lillie applied Nernst's laws to the life phenomena of the *Arenicola*. He produced strong evidence that these are electric phenomena and are dependent, primarily, upon the permeability of the cells. The work of Lillie strongly suggests that the essential phenomena of life are identical with the phenomena of electricity, that is, with variations in ionic concentration and changes in permeability of the semi-permeable membranes — in short, with the reactions of an electro-chemical mechanism. Robertson showed, moreover, that by using oils,

alkalies and acids, most of the cellular phenomena of animals could be reproduced.

After exhaustive studies of nerve currents, Williams and Crehore, making observations with an Einthoven string galvanometer, constructed an artificial nerve which gave convincing evidence that the nerve action current is identical with electricity. An extract from the report of these experiments of Williams and Crehore to the Society for Experimental Biology and Medicine, reads as follows:

"Nearly two centuries ago it was surmised that the nervous impulse might be of the nature of an electric current, but in the absence of definite proof the hypothesis was rejected, especially as objections were raised to it which seemed insuperable. It is difficult, if not altogether impossible, to reconcile all experimental results with the consequences of the molecular theory. If, however, we regard the nerve as an electrical conductor with distributed capacity, we are able to account for many of the fundamental experimental phenomena and also to predict the results of new experimental conditions. It has long been known that the speed of electricity on wires is less than the speed in free space and the formulæ for calculating these velocities are well understood. The rate of propagation of electricity in a conductor similar in form, size and material to a nerve fiber should be, according to these formulæ, of approximately the same order of magnitude as has been measured for the rate of the nervous impulse.

"The enormous reduction of velocity (about ten million times) is chiefly attributable to the great ohmic

resistance of the conductor coupled with the electrostatic capacity. As a result of measurements on the phrenic nerves of cats and calculations based on data of microscopic sections of nerves, we have been able to construct an artificial 'nerve' of glass, paper, tinfoil and graphite, whose total resistance and capacity are of the same order of magnitude as those of the cat's nerve. On applying the break E. M. F. of an induction coil to this artificial nerve and leading off to a string galvanometer in the usual manner we have obtained typical diphasic curves almost identical with those obtained from cat nerves stimulated with the same current. Of greater significance is the fact that we have been able to predict a change in the form of the curves with change in the nature of the applied E. M. F. and to predetermine the character of the change. As an example we may mention that the action current of nerves stimulated by the make or break of a constant current is of totally different form, when registered as a curve, from the diphasic curves obtained by applying a momentary E. M. F.

"It seems at present altogether probable that the phenomena of electrotonus, the effects of lowering of temperature, anesthetics and other well-known phenomena of nerve will be found on investigation to be compatible with the theory that nervous phenomena are essentially electrical in nature."

One of the oldest established facts in physiology is the electric variation in muscle and nerve action. The question has always been: Is this electric phenomenon a result or a cause of action? The work of Crehore and Williams, however, apparently proves that it is

neither cause nor effect, but identical with the action.

Numerous observations made by means of the Einthoven string galvanometer show that there is a quantitative variation in the flow of electricity in muscular activity. There is a rhythmic variation with each heart beat; and there is an intermittent variation in the flow of electricity over the phrenic nerves during respiration. During inhalation anesthesia no electric current can be detected except that identical with respiration and circulation. After death no electric current can be detected. During muscular action the flow of electricity along the efferent nerves is always from the brain toward the periphery. It is evident, therefore, that animals produce electricity; and that in muscular action there is a quantitative flow of electric current along the nerve fibers supplying the involved muscles.

Can electricity alone cause the various organs and tissues to perform their functions? Answer to this query is found in the accepted physiologic fact that adequate electric stimulation of any gland or muscle in the body results in the performance of its normal function.

If the body be operated by means of electric power, then the electricity must be fabricated within the body, which must of necessity then contain mechanisms for the production and storage of electricity, as well as an electro-motive apparatus and provision for maintaining a difference in potential. In short, there should be found in the body a complete electro-motive apparatus, supplying its elements and disposing of its waste matter.

The motor mechanism is readily apparent: the nerve ceptors, contact, distance and chemical; the nerve fibers leading from these to the brain; the nerves leading from the brain to all muscles of the body; the bones and joints; the muscles — these make up the *motor mechanism*. With properly adjusted electric stimulation of the various muscles by means of a faradic battery, there is no doubt that, for instance, the motor mechanism of a dog recently killed could be made to run, to fight, to bark, indeed, to perform every adaptive movement of the body. But these movements would come to an end quickly. The fuel stored in the muscles would soon be used up. The waste products of energy transformation would speedily choke the motor. An automatic mechanism, such as man, must have an automatic arrangement for preventing polarization of the brain battery, for renewing the elements of the battery, for bringing to the muscles new stores of energy and for taking from the muscles the hampering waste matter.

To serve certain of these ends blood has been evolved. Blood floods every cell of the battery and every element of the motor; it carries replenishing stores of energy to the brain and the muscles and brings back the waste products. The mechanisms which prevent polarization of the battery by maintaining the difference in potential, and change the rate of electric discharge and the rate of fabrication of electricity remain to be pointed out.

Granting that in the normal state the battery is not polarized, and that the necessary difference in potential exists, we may assume that the battery in the

human body is, in some respects, like the battery in common use — that is, its loss of difference in potential is due to the action of the battery itself. This being the case, the organs which eliminate waste matter and those which contribute additional energy may be justly regarded as the organs which preserve the difference in potential. As for the organs of elimination, one would expect that for such a large energy transformer as man, the most important organ of the eliminating mechanism would be large in proportion to man's size; that it would have a protected location in the center of the body; that it would have a wide margin of safety to cover the emergencies of life. Furthermore, when this neutralizing organ is excised, the electro-motor would be quickly impaired; fabrication of electricity would quickly be arrested; and the animal, together with the battery, would be "dead." The organ which complies with this description, and is the chief of those organs serving to maintain the difference of potential between the brain and the muscles, apparently is the *liver*. The ultimate and final ejection of the waste products, thus prepared for elimination by the liver, is accomplished by the kidneys and the lungs. In addition to this fundamental work of elimination, the liver also stores fuel — glycogen.

Thus we see that there is in the body an automatic non-polarizable battery, a mechanism for keeping the muscles (the motor) cleared of waste, nerve ceptors specifically adapted to internal and external environmental stimuli, and nerve conductors for transmitting stimuli to the adaptive action patterns in the brain.

In the brain is created not only the electric force that drives the muscles to fabricate heat and motion, but also the electric force that activates certain muscles to assist in the elimination of the acid by-products of energy transformation. To this end, a nerve runs to every muscle which takes part in this elimination, just as to every muscle which takes part in the act of transforming energy. The number of muscles actually engaged in the gross adaptive act are comparatively few; but the muscles engaged in the simultaneously increased actions of circulation, respiration and the elimination of waste matter are many. If a separate impulse were required to go from the brain to every one of the tiny muscles in the walls of the blood vessels and to every cell of the glandular tissues coöperating in the adaptive response, a vast nervous system would be needed.

To obviate this need, there has apparently been evolved an organ, itself under the control of the brain, the secretion of which is capable of mobilizing all the organs and tissues in accordance with the part each is to play in the response. The secretion of this organ increases the action of the brain, raises the blood pressure and accelerates the circulation. It increases the efficiency of the eye by causing the eye to protrude and the pupil to dilate. It probably increases still more the *difference in potential* at the myoneural junction, and facilitates the neutralization of the acids resulting from energy transformation. The action of this secretion, in accordance with what would be most useful in the changeful environment, is quick — almost instantaneous; powerful, but fleeting. *This secretion is adrenin.*

The electric mechanism we have thus far described is wonderfully adapted to the transformation of energy and the elimination of the waste matter resulting from that activity; it responds quickly to every adequate stimulus; but still is a *mechanism which responds at the same rate for all seasons of the year, for all phases of life, for all moments of those phases;* but such a mechanism is not yet a complete adaptive mechanism.

Many periods in the life of the organism require the expenditure of energy at a much higher speed than is required at other periods. In certain seasons of the year, for example, an increased expenditure of energy is needed for adjustment to food supply and climate. In like manner, there are periods of physiological adjustment, such as adolescence, the period of reproduction, courting and mating, and pregnancy; periods requiring sustained physical efficiency, such as the long chase; periods of intense metabolic activity for maintaining the chemical purity of the body, as in infection and auto-intoxication. At such times of "forced draft" on the bodily energies, there is required an organ that will *speed up* the activity of the whole electro-chemical mechanism for the transformation of energy; an organ the secretion of which will act primarily upon the brain, so modifying it that the threshold to all stimuli will be lowered, in order that the brain may drive the body with increased force, and the total output of energy may be constantly augmented. In distinction from the fleeting action of the secretion of the adrenals, the action of the secretion of such an accelerating organ should be slower, steadier and more persistent in its effect.

The one secretion which answers these requisites is the secretion of the thyroid gland. The specific chemical constituent of the thyroid is known. It is iodin. Thyroid extract alone, or iodin alone, causes a steady rise in the rate of energy transformation, a sustained maximum and a gradual fall.

With the brain, the muscles, the liver, the adrenals and the thyroid, we have the essential parts of an automaton, which stores energy in sleep and automatically discharges energy during consciousness; maintains the difference in potential between brain and muscles; mobilizes and demobilizes organs by means of the adrenals; and adaptively varies the speed to accord with seasonal and physiologic vicissitudes by means of the thyroid.

CHAPTER XVI

THE INDIVIDUAL AS AN ADAPTIVE MECHANISM

Having now presented some evidence which suggests the mechanistic character of certain organic processes in man, let us roughly sketch his career as an individual, upon the assumption that he is an adaptive mechanism, dependent for life, as for death, upon the physical conditions of his internal and external environment.

The life of the individual begins with the union of the spermatozoön and ovum. As far as the initiation of development is concerned, this, as Loeb has shown, is essentially a physico-chemical phenomenon. The fertilized ovum may be ejected from the end of the fallopian tube; or, after reaching the uterus, it may be cast off in a hemorrhage caused by a submucous fibroid; in either case, it is a mechanistic end. The fetus may fail to thrive or develop in the uterus of a syphilitic mother the chemical change in whose tissues is produced by a parasite — a spirochete, the activity of which may be checked by a chemical agent — mercury. Again, the life of a fetus in a normal uterus may be terminated if the mother be physically injured or be the subject of strong emotion. In either case, the end is mechanistic.

The life of the individual may be terminated at birth

by any one of many mechanistic accidents. He may be too large to be born naturally, in that event, if no help is at hand, he dies with his mother; or his body may be removed in pieces, that his mother may live. In the violence of birth, a blood vessel in the brain of the child may be ruptured and a clot form; and, in consequence of the continued pressure on the brain by this clot, the growth of the brain may be hindered. The brain being defective, the child — the man — will be permanently defective, and, as such, will be forced to leave the main road of usefulness and happiness and take the byways as a paralytic; — a mechanistic fate. Then again, the blood of a syphilitic mother may impair, but not kill, the offspring, which may be born with the disease, perchance to die early, perchance to share the mechanistic fate of his fellow with the brain clot.

Again the mother of an individual may live in a goiterous region, and in consequence be wanting in thyroid efficiency. The individual, in that event, may be born a cretin. On the other hand, had the mother been given sufficient sheep's thyroid or iodin during pregnancy, she might have borne a normal child instead of a cretin; or the child, if born a cretin, might be made to develop in a normal way by the administration of thyroid extract. All that stands between the stunted, stupid, dwarfed, defective cretin and the normal child is *iodin;* between the syphilitic defective and the normal, *mercury;* between the clot-palsied child and the normal, a *surgical operation.*

If, by chance, the mother of an unborn individual be starved to emaciation, the offspring struggles with the mother against starvation; or if the food of the

mother lacks salt or certain vegetables and scurvy appears, the offspring suffers also. Thus, the simplest mechanistic causes may terminate the life of the fetus or produce a weak or defective child.

The first respiratory movements of the newborn babe are excited by the very delicately adjusted center in the medulla which responds to external stimuli or to slight variations in the alkalinity (H-ion concentration) of the blood, this variation being produced by the asphyxia resulting from the withdrawal of the maternal circulation when the placental structures are separated. With the pressure of the lips of the newborn child against the nipple, the act of sucking is excited. The presence of milk in his mouth excites swallowing; and the entire digestive mechanism is activated by the swallowed milk. Thus the child becomes a breathing, sucking, digesting *mechanism.* Light and shadow and sound soon activate his brain. Each activation of the mechanism for the execution of a given action through contact or distance stimuli facilitates the passage of repetitions of these stimuli, and thus are the first of the vast numbers of *action patterns* formed. In the plastic brain of the newborn babe new action patterns are made during each wakeful moment. Contact stimuli become associated with distance stimuli and associative memory is established.

That the standard of chemical purity in the body may be maintained, the organs of the kinetic system are stimulated to increased activity by the presence of foreign proteins. In like manner, hunger, thirst and cold stimulate the kinetic system to activities by which food, drink and shelter may be secured. Threatened

attack activates the kinetic system for fight or flight. Dust in the nose causes the reaction of sneezing; in the larynx, of coughing; in the eye, of winking. Obstructions of the intestine, of the bile and urinary passages cause expulsion contractions (colic). Injuries of the outer parts of the body cause pain and muscular action.

Implanted in the body are unequally distributed contact ceptors — numerous in areas presented to environment; sparse or absent in protected regions. We find a correspondingly uneven distribution of defense mechanisms against phylogenetic infections and against bleeding; most numerous in the regions phylogenetically exposed to infection and hemorrhage, and sparse or absent from shielded areas. Thus the distribution of the defense mechanisms recapitulates the selective struggle of the organism against its hostile internal and external environment.

The respiratory system, the adrenals and the liver are the principal mechanisms evolved for overcoming the acid by-products of energy transformation. The respiration eliminates carbon dioxid. The liver breaks down the acid by-products thus preparing them for elimination, and the adrenals facilitate the needed oxidation by which this is accomplished. When acid formation is rapid therefore, as in emotion, in fighting, in running, in fever and in Graves' disease, or when acid elimination is defective, as in hemorrhage, asphyxia, failure in circulation, the late stages of diabetes, of cardiovascular disease or of Bright's disease, and in cases of liver insufficiency; or when acidity is induced by ether, chloroform or nitrous oxid, the respira-

tory rate is increased through the specific stimulation of the respiratory center by the increased H-ion concentration. The kinetic system is driven only by the higher centers of the brain. They alone control the adaptive transformation of energy. Increased H-ion concentration diminishes and even arrests the driving power of the brain; that is, it inhibits the higher centers and stimulates the respiratory and other acid-neutralizing mechanisms. This antithetic reaction of the acid-producing part of the brain and the acid-eliminating part of the brain prevents death by acidosis during muscular exertion, emotion and fever.

If, however, we give an individual deep narcotization with morphia before he is given the adequate stimulus to emotion, exertion or fever, we find there is little or no transformation of energy, and his brain-cells, adrenals and liver remain histologically normal. Morphia performs a physiologic decapitation, completely neutralizing the effect of the crushing injury, the overwhelming danger, or the powerful infection. As a corollary, we find that, if decreased alkalinity be present either as a result of energy transformation, of inhalation anesthesia or of some other cause, then large doses of morphia hinder or prevent the return of the blood to its normal alkalinity. Strychnin and iodin are antithetic to morphia, the first causing convulsions and the second causing the kinetic drive of fever, emotion or exertion. Whatever causes excessive energy transformation diminishes the alkalinity of the blood and causes an increased output of adrenin, mobilizes thyreoidin and glycogen and by increasing the electric output of the brain leads to physical exhaustion and

identical histologic lesions in the brain, adrenals and liver.

If, instead of an increased transformation of energy through a short period, an individual be subjected to a prolonged period of increased transformation of energy from the diverse causes already mentioned, then we find changes of great significance in the organs of his kinetic system. The thyroid may become hyperplastic, as in the case of prolonged infection, pregnancy, auto-intoxication and sexual excitation. In animals and in man, likewise, we frequently find the adrenals enlarged in the breeding season, in pregnancy, in cardiovascular disease, after or during chronic infection; while injections of indol, skatol, leucin, tyrosin or peptone, intense fear and excessive muscular exertion cause an increased output of adrenin. In these states, also, the adrenals contain less adrenin, and the liver less glycogen than in the normal state.

During pregnancy many organs undergo structural changes. The mammary glands enlarge; the thyroid, adrenals, brain and liver show increased activity in the transformation of energy and in the neutralization and excretion of acid by-products. In some instances, the organs of neutralization and excretion prove inadequate; and in consequence, there result nephritis, high blood-pressure and rapid respiration, and finally eclampsia and death. If, however, the fetus be removed, the symptoms at once disappear; a phenomenon as clearly mechanistic as the cure of auto-intoxication by freeing the intestines of their poisonous contents; as mechanistic as the amelioration of Graves' disease by the excision of the hyperplastic lobe of the

thyroid; as the relief secured for an overworked man by rest, or for the harassed individual by substituting hope for fear. All these are mechanistic phenomena in the life career of man as an individual.

We have pointed out incompletely and imperfectly the mechanistic rôle played by the organs and tissues of the body in transforming the energy needed for the daily routine of life, and in maintaining the chemical purity of the body, especially when excessive metabolism results from intense emotion, infection or muscular exertion. Let us now briefly consider how the individual, like other mechanisms, is modified by the impairment or the deprivation of certain parts.

Excision of Organs

Brain: When the *brain* is progressively destroyed by cerebral softening, the conversion of energy in muscular action and fever is correspondingly diminished. When a certain percentage of brain-cells has been lost, then the brain can no longer adequately drive the body and a state of equilibrium is reached — the individual is dead. If the cerebral hemispheres and the cerebellum are removed from an animal, it may live for months or years, but it cannot respond to stimuli affecting the distance or contact ceptors. That is, it possesses no associative memory. A decerebrate infant is short-lived. An individual with a defective brain — an idiot — may live for many years, but his activities are limited. The function of the brain may be depressed or even temporarily suspended by morphia, acidosis, fever, emotion, exertion or physical

injury. In each case, the reactions of the individual as a whole are correspondingly limited.

The Muscles: If the function of the muscles is lost or hindered, the reactions of the individual may be as greatly affected as by depression of the function of the brain. If the muscles are disconnected from the brain by severing the connecting nerves, or if the function of the muscles is suspended by curare, the individual will be as helpless as if his brain had been removed. For a time, his life may be prolonged by artificial respiration; but he can move no muscles; he can produce only a negligible amount of heat; he is powerless, dumb and cold—little better than dead. We see, therefore, that the muscles bear just as mechanistic a relation to the work of the individual as a whole, as the motor of an automobile bears to the reactions of the whole machine.

The Adrenals: Excision of the adrenals causes a progressive decline in muscular power and in the production of heat until death, which inevitably occurs within a few hours. The H-ion concentration of the blood increases progressively with the approach of death.

The Thyroid: The excision of the thyroid in carnivora and in man causes a rapid diminution of muscular power and a diminution in the production of heat. Sexual desire and procreation are depressed or lost; the mind is weak; the individual becomes large, flabby and stupid — a repulsive human caricature. Feeding thyroid extract to such an individual transforms him into a comparatively normal physical and mental being — a markedly mechanistic phenomenon.

The Liver: Excision of the liver causes within a few hours a rapid decline in muscular power and in heat production until death. Before death the H-ion concentration of the blood increases rapidly.

Testicles and Ovaries: Excision of the testicles and ovaries, before adolescence, prevents the development of the secondary sexual characteristics and prevents sex reactions and procreation.

Pancreas: Excision of the pancreas interferes with sugar metabolism.

Thymus: Excision of the thymus interferes with the growth of the skeleton.

Hypophysis: Excision of the hypophysis interferes with growth and with sugar metabolism, while excessive hypophyseal secretion causes excessive growth (gigantism).

Parathyroids: Excision of these two tiny bodies interferes with calcium metabolism and may cause death by convulsion (*Calcium tetanus*).

All these defects support a mechanistic conception.

Want of Certain Chemical Elements

The human mechanism may be modified not only by the loss of some of its component parts but also by depriving the body of certain food constituents. For example, the exclusion of sodium chloride from the diet soon causes death, and the removal by milling of vitamin, a tiny element in the husks of rice, has caused the death of multitudes of rice-eating people and is the cause of the disease known as *beri-beri.* The administration of this minute constituent of rice prevents and cures *beri-beri* (Craemer).

While this list is by no means complete, we have mentioned some organs and some chemical substances the removal of which handicaps or destroys the individual. These organs and chemicals are purely material things, purely mechanistic in their action. We thus see that, at will, by depressing or removing this or that organ, by administering this or that external agent, muscular power and the production of heat are diminished or lost; the action of the brain may be gradually depressed until unconsciousness and death is reached. It would seem that while a man-made machine is apparently, it is not really, more dependent on chemistry and physics than is that complex animal mechanism, *man*.

We have now followed, though imperfectly, the career of the individual from his beginning in fertilization, through the unconscious fetal days and the hazards of birth to his conscious adult life. We have seen him struggling to adapt himself to his environment in infancy and in childhood and during adolescence. We have seen his kinetic system driven by injury, by emotion, by infection; and have seen many diseases result from his struggle with his internal and his external environment. We have seen him complete the cycle of life through procreation. We have seen that his death results from a vital break in his mechanism, and that his ashes are returned to the elements whence they came. From conception and birth to death, we have seen that virtually every phenomenon of life is mechanistic. We have studied the imperfect record of the ascent of man's species from the time when, having been driven by powerful enemies to the trees,

he evolved his strategy and acquired hands, which later enabled him to fashion weapons; to the period in which he returned cautiously to the hostile ground of his ancient enemies and with better strategy resumed the battle by using the forces of nature; to the period in which he discovered fire, fashioned simple tools and weapons, made dugouts, tamed animals and planted seeds, thus making nature herself aid him to obtain food and shelter and protection against his foes. We have seen increased power accrue to man coincidently with the development of spoken and written language from mere symbols of communication. We have seen that as man became more and more completely adapted to environment, his numbers increased, until, in his desire to possess the earth, he found his most formidable enemies to be his fellow men; and hence, with the blood of man shed by man the earth has been deluged. We see that this human animal is exceedingly prone to kill, because his evolution has depended upon his ability to conquer brute animals and his fellow man. We see that his two most complete adaptations are those of killing and procreating — the inevitable sequel of the primal needs for self-preservation and for the preservation of his species.

The most powerful activator of the kinetic system of man to-day is his fellow man. This is the enemy he most fears. In the midst of plenty he strives for more. He is at war with his fellows in business, in education, in the arts, in the professions, in philanthropy and in winning mates. There is no game nor sport that is not a battle. Even the toddling child, when pursued, turns at bay when captured; an ob-

vious recall of the bloody abyss of phylogeny, since all animals turn for the final death struggle. In all his waking moments, and even in his dreams, man exerts himself against his fellows. He fears; he hopes; he triumphs; he is vanquished; he is jealous and suspicious. Yet with all his fears and struggles, he is forever bound to his fellows by the chains of necessity, for he cannot succeed alone. Man is, of necessity, a gregarious animal. He hates and fears, while at the same time, he is grateful and dependent. The rivalry and jealousy of his life turn to grief at the death of his rival. And in these emotions and strivings are laid the foundations of many diseases. These antithetic relations between individuals are exhibited on a vast scale by nations in mutual dependence, mutual help, mutual jealousy, mutual hate, mutual efforts to kill.

The effect of fear, grief, worry and jealousy on the physical body is seen in the changes in the cells of the brain, the adrenals and the liver, and in the numerous resultant diseases and disabilities. Against man's inhumanity to man, religions and philosophies have been evolved, each of which aids in proportion to its power to substitute altruism for selfishness, to substitute faith for fear. Thus in understanding the physical basis of the action of faith and hope, as opposed to fear, despair, anger and grief, we have at our command a concrete force which can be efficiently used to protect the individual. As the knowledge of disgrace and punishment prevents dishonesty; as the knowledge of contagion prevents exposure to contagion, so the mere knowledge — the conviction — that excessive anger, work, jealousy, envy, worry or grief cause physical

damage as serious as that produced by infections or crushing blows will constitute a powerful protection to man. The knowledge that these activations not only decrease the power of the individual to do his work, but ultimately cause numerous diseases as well, will result automatically in arousing the instinct of self-preservation, which will surround the individual with a protecting circle, through which anger, jealousy, grief, and worry cannot penetrate, just as the zone of local anesthesia in the anociated surgical operation is an impenetrable barrier between the brain and the knife, making the surgical operation shockless.

In the texture and form of his bones and joints; in the structure and distribution of his muscles; in the covering skin and the padding fat; in the nature and distribution of his nails and hair; in the structure and equipment of the mouth, the stomach and the intestines, of the kidneys, ureter and bladder and of the organs for procreation and respiration; in the composition and circulation of the blood; in the distribution of pain ceptors, and of the defense mechanisms against dust, débris and insects, against cold and heat, and against infection and bleeding; in the mechanisms for appreciating sound and light, color and form; in the mechanisms for taste and for smell, for maintaining an even body temperature, for producing muscular action and for expressing the emotions; in the nature and incidence of laughter and weeping; in the chemical defense against bacterial invasion and against the poisons of pregnancy and auto-intoxication; in the mechanisms of conception, of pregnancy and of birth; in the fabrication of thought; in the mechanisms of

communication by natural, spoken and written language; in health and in disease — in the complete life cycle of the individual from conception to death we see clearly here and dimly there the mechanisms by means of which a sensitive being immersed in a hostile environment effects survival, — we see man — an adaptive mechanism.

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